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ON THE CLINICAL ASPECTS OF PLAGUE.[1]

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As the time allotted to this discussion is necessarily limited to a few minutes, I shall confine my remarks chiefly to the characterization of the clinical types of plague and to the diagnosis of the disease rather than enter upon an analysis of the individual symptoms. The statements are based upon a clinical study of plague made in San Francisco[2] in February, 1901, and previously in 1899, in Hong Kong and in India (Bombay, Poona). The descriptions are based upon the conception that plague is a disease due to infection with a bacillus (B. pestis), which is capable of causing acute general septicæmia without visible local reaction in highly susceptible animals, or a local process (usually manifested in the nearest lymph glands rather than at the site of inoculation) in resistant animals, or processes intermediate in severity in animals intermediate in resistance.

The first case of plague was discovered in San Francisco on March 6, 1900, by Drs. F. P. Wilson and W. H. Kellogg, the diagnosis being confirmed by animal experiment by Dr. J. J. Kinyoun, of the United States Marine Hospital Service. There are indications that the disease has existed even longer, but the proof for this can scarcely be brought. In all probability it came to San Francisco from Hong Kong or Canton, and is accordingly to be looked upon as an offshoot of the Chinese epidemic. The disease in San Francisco has at no time prevailed in the form of an outspoken epidemic, the mortality tables not being conspicuously altered by its presence:

[1] Based on remarks made before the Association of American Physicians, Washington, May 1, 1901.

[2] As a member of a Commission appointed by the Secretary of the Treasury under the orders of the Surgeon-General of the Marine Hospital Service.

MORTALITY FROM ALL CAUSES AMONG CHINESE OF SAN FRANCISCO, 1897–1901.

Months.	1897	1898	1899	1900	1901	Months.	1897	1898	1899	1900	1901
January,	37	35	46	64	45	August,	35	47	43	19	
February,	46	36	39	48		September,	45	27	35	27	
March,	38	46	37	47		October,	36	53	44	32	
April,	35	41	33	30		November,	39	66	37	34	
May,	27	34	36	42		December,	23	46	48	32	
June,	30	21	46	25							
July,	39	25	34	38		Total,	430	477	478	438	45

On the contrary, the progress of the disease in California has been that which has characterized plague before the outbreak of a great epidemic in nearly every place where the disease has prevailed. It is the same kind of "sneaking" progress as was seen in Hong Kong, Calcutta, and Bombay for months before large numbers of people were attacked. That such "sneaking" epidemics may die out without culminating in a large outbreak was demonstrated by the experience in Ahmedabad from October, 1896, to August, 1897, where, though one hundred and thirty-six cases of plague were imported, the disease developed in only twenty-seven of the inhabitants.

In connection with the fact that no great outbreak has occurred in San Francisco, it is significant that as far as ascertained there has been no general infection of the rats of that city. A small number of rats found dead, as well as several living rats caught in the sewers of Chinatown, showed no evidence of infection with bacillus pestis.

Up to the time of our visit to San Francisco twenty-five deaths due to plague had been discovered during a period of about eleven months (March, 1900, to January, 1901). These cases have been reported by Dr. Kellogg,[1] and it is from his reports that I have drawn the data referable to the cases which occurred before February, 1901. During the eight days—February 6 to February 13, 1901—the special commission from the Treasury Department found six cases of plague. Altogether, then, from March 6, 1900, to February 13, 1901, thirty-one cases of plague had been recognized. Most of them were found dead, and the diagnosis was based upon the pathological appearance and the bacteriological examination. Several cases were, however, studied during life. Of the six cases observed by the Commission, three were seen during life, and two of these three recognized clinically as cases of bubonic plague.

[1] Kellogg, W. H. The Plague: Report of Cases, Occid. Med. Times, S. F., 1900, vol. xiv. pp. 197–207. Kellogg and Kinyoun, J. J. The Plague: Thirteenth Case, ibid., 1900, vol. xiv. pp. 245–257. Kellogg, W. H Plague Cases Fourteen and Fifteen, ibid., 1900, vol. xiv. pp. 284–85. The Plague in San Francisco, Cases Sixteen, Seventeen, and Eighteen, ibid., 1900, vol. xiv. pp. 345–47. Plague in San Francisco, ibid., 1901, vol. xv. pp. 11–15. Plague Cases Twenty-three, Twenty-four, and Twenty-five, ibid., 1901, vol. xv. pp. 45–46.

No.	Name.	Age.	Sex.	Color.	Place of death.	Date of death.
1	Wing Chut King,	41	M.	Mongolian,	1001 Dupont,	Mar. 6, 1900
2	Chu Gan,	22	M.	"	723 Sacramento,	" 15, "
3	Ng Ach Gin,	37	M.	"	905 Dupont,	" 17, "
4	Lee Sun King,	47	M.	"	Oneida Place,	" 18, "
5	Law An,	38	M.	"	St. Louis Alley,	Apr. 24, "
6	Lim Fa Muey,	16	F.	"	789 Clay,	May 11, "
7	Chu Sam,	38	M.	"	717 Jackson,	" 11, "
8	Chin Moon,	16	F.	"	730½ Commercial,	" 13, "
9	Her Woon Jock,	53	M.	"	740 Pacific,	" 14, "
10	Dang Hong,	40	M.	"	706 "	" 29, "
11	Chen Kney Kim,	49	M.	"	819 Clay,	June 2, "
12	Jay Man Tong,	60	M.	"	759 "	" 9, "
13	Lee Wing Tong,	40	M.	"	767 "	July 6, "
14	William Murphy,	34	M.	White,	427 Dupont,	Aug. 11, "
15	Ham Tan,	29	M.	Mongolian,	900 "	" 15, "
16	Lee Do Hen,	50	M.	"	710½ "	Oct. 5, "
17	Chun Yen,	37	M.	"	767 Clay,	" 10, "
18	Taik Dong Leong,	39	M.	"	705 "	" 14, "
19	Young Moon Li Chee,	30	F.	"	802 Dupont,	" 31, "
20	Young Wah Noui,	9	F.	"	802 "	Nov. 1, "
21	Anne Roede,	28	F.	White,	Pacific Hospital.	" 3, "
22	Lee Ho,	30	M.	Mongolian,	844 Washington,	Dec. 7, "
23	Chun Wey Lung,	60	M.	"	780 Jackson,	Jan. 6, 1901
24	Leam Wing Low,	59	M.	"	683½ Clay,	" 15, "
25	Angela Colombo,	...	M.	White,	5 Lafayette Place,	" 15, "
26	Chun Ah Chou, *a*	44	M.	Mongolian,	814 Washington,	Feb. 5, "
27	Lum Hong Yuen, *a*	37	M.	"	28 Ross Alley,	" 6, "
28	Wong Chi Lui, *a*	50	M.	"	15½ Waverley,	" 7, "
29	Tom Shom, *a*	51	M.	"	814 Washington,	" 10, "
30	Ungh Ah Buck, *a*	45	M.	"	St. Louis Alley,	" 11, "
31	Foong Ah Fong, *a*	12	F.	"	747 Sacramento,	" 12, "

a Observed by Commission.

NOTE.—Particular places of death of following numbers were as indicated below: No. 8, Pacific Hospital, Stockton and Chestnut Streets; No. 13, City and County Hospital; No. 14, City and County Hospital; No. 21, Children's Hospital, 3700 California Street; No. 25, City and County Hospital.

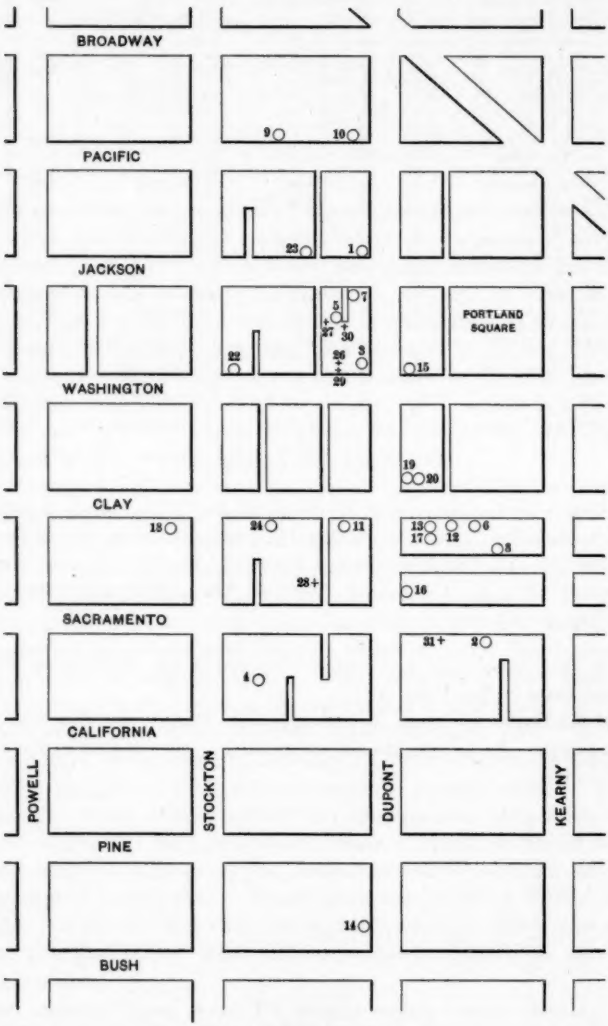
The accompanying map (page 380) shows the distribution of the plague cases in San Francisco:

Of the thirty-one cases, twenty-eight were Mongolians and only three Caucasians. As to age, the following table gives the deaths according to decades:

Age.	Deaths.
1 to 10 years	1
11 " 20 "	3
21 " 30 "	5
31 " 40 "	9
41 " 50 "	7
51 " 60 "	5
61 " 70 "	0

As is well known, plague usually kills more people between twenty and thirty than in any other decade. It is to be remembered, however, that in San Francisco the Mongolian population may scarcely be regarded as a normal one. The number of females is small, there are relatively few births in Chinatown, and relatively few young people.

The predominance of males and middle-aged individuals is easily explicable when the legal status of the Chinese in America is considered.



Map of "Chinatown," San Francisco.

Circles indicate cases seen and regarded as plague by City Board of Health before arrival of Commission.

Crosses indicate cases of plague observed by the Commissioners from February 5th to February 12, 1901.

Of the thirty-one cases, six were in females and twenty-five in males. Experience in other epidemics indicates that there is but little difference in the number of males and females attacked. The disproportion in the San Francisco epidemic is doubtless dependent upon the small number of female Chinese living in Chinatown.

The type of the disease which has been prevailing is the bubonic. In twenty-three of the thirty-one cases a definite bubo (probably primary) was made out in twenty-three instances. Only one primary septicæmic case was established, and only one pneumonic case was observed. In seven of the cases the descriptions do not permit of definite classification as regards the clinical type, though the diagnosis of the disease itself was in each case fully established.

The daily inspections of the sick and dead permitted of observations relative to the mode of life of the people in the fourteen blocks of San Francisco which make up "Chinatown." These observations were extended by special trips of inspection under the guidance of officers of the city detective force and by numerous independent trips of inspection.

The dwellings of the poorer classes of Chinese were found to be here, as they seem to be everywhere, shockingly unsanitary. In places there is marked overcrowding; the rooms are small; they are often entirely devoid of light or means of ventilation, and nearly always insufficiently lighted and ventilated; many of them are filthy; some of them, especially those situated in basements, are damp, and emit a foul stench. These faults in sanitation are not confined to the tenement-houses of the Chinese; on the contrary, in the rear of or over or under some of the more pretentious business buildings are to be found sleeping and living apartments which are most objectionable from a sanitary point of view.

The Chinese in San Francisco are, however, in many respects much better off than are their countrymen in great native centres like Canton, or even than those in a city like Hong Kong. There is almost an entire absence of the utter destitution met with among many of the Chinese in Asia. The Chinese in San Francisco are, on the whole, very well fed, for wages are high and food is abundant and cheap. They are also well clothed, as a rule, and particular emphasis is to be laid upon the fact that the Chinese here wear shoes, stockings, and trousers, since it is believed by many that the bare legs and feet of the Chinese in Hong Kong and Canton had much to do with the frequency of infection with plague in those places.

A large percentage of the Chinese in San Francisco, it is said, smoke opium. There are a number of Chinese prostitutes, but inspection of the quarters occupied by the latter would indicate that the rooms in which they live are, on the whole, more wholesome as regards air-space,

light, ventilation, and cleanliness than those of the other inhabitants of the district.

The Bubonic Cases or Glandular Plague.

The ordinary clinical features of this form are now so familiar that they need scarcely be entered into in detail. The symptom-complex is characteristic, and there ought to be but little difficulty, as a rule, in making a diagnosis. The sudden onset of fever, preceded, usually, by but few prodromata, associated very quickly with painful glandular enlargements, severe headache, nausea, and vomiting are the conditions commonly met with. The fever varies between 103° and 105° F., but may rise as high as 108° or even higher. There is a moderate leucocytosis associated with some anæmia, and with a moderate diminution in the amount of hæmoglobin.

The buboes usually appear rapidly after the first onset of symptoms. Indeed, if a physician is called he nearly always finds a bubo already developed. The size varies according to the stage of development of the bubo and the character of the infection. Usually one gland of a group swells first, after which there is rapid extension to other glands of the packet. The larger buboes are due to swelling of several glands and œdema of the adjacent tissues. In the fully developed buboes it is usually impossible to make out the individual glands of which the whole swelling is made up. The buboes are exquisitely painful, as a rule, though some lethargic patients complain but little. They are especially sensitive on pressure. Among the Chinese it was common to find a black plaster applied to the region of the swollen glands, to alleviate what the patient regarded as "rheumatic" pain. A good deal of stress is to be laid upon the elastic resistance of the swelling, which is due to the œdema. The skin may be tense over the swelling; it looks thin and glossy. It is often reddened over the bubo, and occasionally vesicles or pustules appear on the surface. In very large buboes, especially in the cervical region, the jelly-like trembling which has been described can easily be made out. If the œdema becomes very extensive the bubo may be obscured. Most patients assume the attitude best calculated to relieve the tension in the region of the bubo; thus, where the bubo is inguinal the leg is flexed at the knee and the thigh moderately flexed and rotated outward.

As Müller and Pöch have pointed out, the clinical classification of buboes differs of necessity somewhat from the classification based upon the pathology of the disease.[1] The pathologists distinguish primary buboes of the first order, primary buboes of the second order, and secondary buboes, the first group including the buboes appearing in the

[1] See Dr. Flexner's report.

glands nearest the site of inoculation, the second group including the buboes formed by extension of the bacilli directly through the lymphatics from the primary bubo to a second adjacent group of lymph glands, and the third group including buboes arising through the deposition of bacilli from the circulating blood in lymph glands in any part of the body. Clinically, it may be very difficult or impossible to distinguish primary buboes of the second order from secondary buboes. We are reduced to distinguishing the "clinically primary" bubo from the "symptomatic" bubo. The clinically primary bubo is nearly always a primary bubo of the first order. The symptomatic buboes may be primary buboes of the second order or true secondary buboes.

In a suspected case of plague it is necessary to search widely for a primary bubo. If it is not easily found, one should examine every part of the body in which lymph glands are situated before concluding that no primary bubo is present. It is probable that there are some primary buboes too small to be recognized clinically, though it is more likely that in many instances the smaller buboes which could have been detected by careful search have been overlooked. In the bubonic form death occurs usually in from four to six days. In San Francisco we got histories of a much longer duration in several cases. Where the disease is prolonged suppuration may occur. A striking feature of the disease is the absence of lymphangitis between the site of inoculation and the lymph gland attacked. It is rare that one can make out the point of entrance of the virus, though occasionally a vesicle or a pustule exists, the so-called primary skin lesion in the bubonic form of the disease.

The inguinal type of glandular plague was much more common in San Francisco than the axillary and cervical types, and this is in accord with general experience. As an example of typical inguinal bubonic plague, the following instance may be cited:

Tom Shom, male, aged fifty-one years, actor in Chinese theatre; room above theatre at 814 Washington Street, near room of late Chun Ah Chou (see death 26). This man was reported as ill to the Six Companies, and was examined clinically on Friday, February 8th, by the writer, who obtained the following history: The man had been acting in the theatre about two weeks before, although it had been stated that he had not been very well for from six to seven months previously. On February 4th he became seriously ill with fever and delirium. There had been some vomiting. The urine, as observed by the attendant, was described as brandy colored. He had a Chinese doctor in attendance, and his friends had not considered him ill enough to make a report to the Six Companies worth while. The man smoked about fifty cents' worth of opium daily. On clinical examination the patient was found lying upon his back in bed, with legs drawn up; he was in a state of semi-stupor. His pulse was 108, quick, rather full, but of low tension. The skin was hot and dry; respiration 20 to the minute.

The face had an anxious expression; the tongue was coated in the middle. There was no palpable enlargement of the glands of the neck or axillæ, but in the right groin several slightly enlarged glands could be distinctly felt, and the patient, though his mind was partially clouded, winced decidedly when either groin was palpated. It was evident that the glands were quite tender. In the absence of urethral discharge, chancre, or evidence of local irritation in the lower extremities, the case was, on account of the local and general phenomena, regarded as one of plague. The skin was cleansed and a sterilized hypodermic needle introduced into the groin. A few drops of bloody fluid were withdrawn, presumably from one of the enlarged glands. It was difficult to be sure of this, however, as the patient could not be kept quiet while the needle was being inserted. No colonies of plague bacilli developed in the inoculated tube. The necropsy, subsequently made, indicated that the needle had failed to enter an enlarged gland.

The patient was seen on the following day, when his condition showed no change for the better. The pulse was 136 and feebler, the patient seemed in general weaker, and an unfavorable prognosis was made. The patient's friends were told that an injection of Yersin's serum offered the best chances for recovery, though they were also told that not much could be hoped from any treatment in the stage of the disease in which the patient then was. The offer was refused. The man died on February 10th, the next day.

The dead body was inspected on the morning of February 11th. The body was in a state of firm rigor mortis, the limbs being strongly flexed. On breaking down the rigor mortis and palpating the glands in the groin, it was difficult to say positively that there was any enlargement of the lymphatic glands In view of the enlargement distinctly made out during life and the clinical picture which had been observed, the death was believed to be one due to plague, and a pathological and bacteriological examination undertaken.

At autopsy there was a slight swelling in the right inguino-femoral region, which, on incision, revealed slightly œdematous subcutaneous tissue, with slight enlargement of the glands. The largest gland was the size of a filbert, and its surface was dark and hemorrhagic; on section, it presented distinct hemorrhages; other glands were swollen, soft, juicy, and hemorrhagic. The spleen was enlarged, soft, and friable. The examination of the groin showed that the hypodermic puncture made for the withdrawal of fluid for diagnostic purposes during life had failed to enter a lymph gland.

Cover-slips from the spleen and glands showed large numbers of bacilli having the characteristic properties of the B. pestis.

Sometimes these inguinal cases are associated with a marked hemorrhagic diathesis. This existed in the case of W. M.,[1] who died on August 11, 1900.

M. was a white man, aged thirty-four years, who on August 7, 1901, complained of pain and slight swelling of the right groin, followed by nausea, general soreness, headache, and vomiting. He had albumin in urine, his temperature was 100°, pulse 100, and the bubo in the right

[1] See Dr. Kellogg's report.

femoral region became rather painful. Died on August 11th. Autopsy by Prof. Taylor. Two enlarged lymph glands were found in the right groin. These were hemorrhagic, but not purulent. The femoral glands were also enlarged. The plague bacillus was present in smears made from the glands, and animals inoculated therefrom died with typical plague lesions. The mesentery was mottled with hemorrhages. The walls of the stomach were markedly injected, and there were submucous hemorrhages in this organ. The spleen was very friable. Extensive hemorrhages were found about the pancreas, in its substance, and in the lesser peritoneal cavity. There was no fat necrosis.

Axillary buboes were not met with during the stay of the commission in San Francisco, nor do they appear to have been seen by San Francisco clinicians. In view of the experience in India and China, where axillary buboes are much more common than cervical buboes, it would seem possible that the axillary buboes, possibly of small size, had been overlooked in some cases in San Francisco. Axillary buboes are, however, more common in women than in men, and the small number of women in San Francisco may have had something to do with the non-discovery of axillary buboes.

Cervical buboes come next in frequency. They are usually very large and painful. The œdema is extensive, and there is often difficulty in swallowing. A typical case was seen by the Commission on February 12th:

Ung Ah Buck, aged forty-five years, found dead at Wing Hai's undertaking establishment, on Sacramento Street. This man had been seen alive and examined by the writer on the previous day, who diagnosed the case, *intra vitam*, as one of cervical bubonic plague. When seen alive he was in a room upstairs in the rear of 921½ Dupont Street, opposite St. Louis alley. The man was sitting up, but looked extremely ill. His face was pale, cyanotic, and anxious-looking. His voice was very feeble, but his intelligence seemed almost unclouded, and he was able to carry on a conversation, though with difficulty, with the interpreter. The friends stated that he had at times wandered in his talk. He was under the care of Dr. Mather. The patient stated that he had been ill for two weeks. His neck had been swollen for one week, and he regarded the condition as quinsy. With the aid of a tongue depressor the throat was examined. The fauces were swollen and reddened, the swelling being very marked in the left side. The left palatine tonsil was much enlarged and showed on its surface a grayish-white patch the size of a dime. The reddening in the throat was general, and there was less local injection than one ordinarily sees in diphtheria. The left side of the neck was brownish-yellow, having been painted over with a solution of iodine. On inspection and palpation marked bulging was found. This seemed to be due to enlargement of the cervical lymphatic glands. The case was diagnosed as one of plague, with cervical bubo. The man died the next day, and a complete autopsy was made by Dr. Flexner. The pathological examination showed typical lesions of plague, and the bacteriological examination made by Dr. Novy demonstrated the presence of B. pestis.

Autopsy, February 12th at noon, at the undertaking shop of Wing Hai, by Dr. Flexner, Drs. Novy, Barker, Kellogg, and Wilson being present. The left side of the face and neck presented a marked diffuse swelling, extending from the angle of the jaw backward to the sterno-cleidomastoid muscle and below, almost reaching the clavicle.

On incising this region the parotid gland was first reached; this organ presented a normal appearance. After dissecting away the parotid gland a group of greatly enlarged deep glands surrounding the carotid artery and jugular vein came into view. The periglandular tissue was infiltrated with bloody fluid and presented a sodden appearance. The enlarged glands and portions of the surrounding tissue were excised; the former were found to be swollen (several reaching the size of an English walnut) and to be wholly altered in appearance and consistence. In color they were deep purplish, and on incision a hemorrhagic fluid exuded. Opaque points of necrosis were also present.

The general subcutaneous fat was well developed; there was no general œdema. Peritoneum appeared smooth and glistening; there was no excess of fluid in abdominal cavity, and the abdominal glands were not noticeably swollen. The spleen was enlarged to fully twice its normal size; it presented a purplish color, and its consistence was diminished. The pleural cavities were dry. The lungs retracted moderately upon removal of the sternum. The lower lobes of the lungs were congested, but no consolidation was made out. No other abnormality was observed in the body.

The organs and tissues removed at this necropsy, consisting of the enlarged cervical glands and spleen, were taken to the laboratory, where cover-slips, cultures, and animal inoculations were made.

The cover-slips from the spleen showed large numbers of a bacillus having the morphology and staining properties of the B. pestis. The cover-slips from the glands differed in their appearance. In some instances there were present large numbers of bacilli similar to those in the spleen, together with a few diplococci or short chains of cocci. Other cover-slips showed, beside the organisms mentioned, a bacillus having the morphology of the B. diphtheriæ. Animals inoculated died with typical plague lesions, and pure cultures of the B. pestis were obtained from them.

Cubital and popliteal buboes were not met with in San Francisco.

Symptomatic buboes were seen in several cases. On autopsy these proved to be in some instances primary buboes of the second order, in other instances true secondary buboes.

The Septicæmic Cases.

The more one studies plague the more he is impressed with the resemblance of plague infections to those which occur in anthrax. It has been doubted by some, among them no less acute an observer than Müller, whether primary plague septicæmia occurs without any primary bubo. It is easy to say when no primary bubo is found in a case of plague septicæmia that the pathologist has overlooked the primary bubo at autopsy, but autopsies have been made by very careful path-

ologists in which no definite primary bubo could be made out. And it would seem that we are as much justified in assuming the existence of a primary plague septicæmia as of any other form of primary septicæmia. Terminal plague septicæmia in fatal cases of the bubonic form, and probably of other local forms of disease, is far more common. Between a plague septicæmia, primary from the first, and the terminal plague septicæmia secondary to primarily localized plague infections, various transition forms are met with.

Primary Plague Septicæmia. One can think of the bacillus getting into the blood in cases of primary plague septicæmia in various ways. When a human being or an animal is extremely susceptible it is conceivable that the bacillus could enter through the skin and pass through the lymph glands, and so into the blood without setting up a primary bubo. In the same way it could enter through the conjunctiva or other exposed mucous membranes. It is possible that entrance could occur from the respiratory tract without setting up local pulmonary lesions other than a mild bronchial catarrh, and, finally, direct infection of the blood through the bites of insects may be thought of.

In primary plague septicæmia the clinician has to deal with the phenomena of general septic infection; the fever is high, the pulse is frequent and feeble; there may be delirium and coma. A splenic tumor rapidly develops, and is often associated with acute pain in the left side. There is tenderness over all the lymph glands of the body. Frequently there are hemorrhages into the skin or from the mucous membranes of the lungs, stomach, intestines, or urinary passages. In such cases the bacilli can frequently be found in cover-slips made from the blood; cultures from the blood are, however, more reliable for the discovery of the bacilli, and animals inoculated with a few cubic centimetres of blood die with typical lesions of plague. These primary septicæmic cases include many of the frightfully acute infections met with in large epidemics; death may occur in from one to three days from the time the patient is first attacked or even after the lapse of a few hours.

In San Francisco a white nurse died of what appears to have been this form of the disease. She was taken suddenly ill, complaining of severe pain all over the body. Her temperature was 40° C., pulse 104, respiration 33. There were hemorrhages from the urinary passages and the sputum was bloodstained. Hemorrhagic petechiæ were found about the elbows and ankles. She died in the hospital, and an autopsy was made by Dr. Harold Bruhn. The inguinal glands were slightly but not markedly enlarged. The axillary and cervical glands were not large. There was some free blood in the pelvic peritoneal cavity. In the mesentery the glands were slightly enlarged. No pulmonary lesions were found. The spleen was enlarged and softened. There were subperitoneal hemorrhages, and submucous hemorrhages in

the intestine. The pathological diagnosis was septicæmia, with tendency toward minute hemorrhages in the tissue. Bacteriological examination proved that the blood was full of bacilli of plague, and there were enormous numbers of the plague bacilli in the spleen.

Secondary Plague Septicæmia. It seems likely that in nearly all cases of bubonic plague at least a few bacteria get over into the blood. It is these which account for the true secondary buboes which are regarded by the pathologists as being embolic in origin. In many of the fatal cases of bubonic plague the bacteria go over into the blood and multiply in great numbers, so that the blood and spleen at death and shortly before contain large numbers of the plague bacilli. In cases of the bubonic form of the disease which recover it may be that such a general bacteræmia does not occur, the process remaining essentially localized to the primary buboes, or, if a few bacilli get over into the blood, they are filtered out by the organs, and give rise to either secondary buboes or to no noticeable phenomena.

Plague Pneumonia.

Primary plague pneumonia is to be distinguished from the secondary pneumonias which occur in the course of other forms of infection with plague. By primary plague pneumonia is understood that form in which the bacillus gains entrance to the body through the respiratory tract, and sets up a definite primary pneumonia, usually lobular, but sometimes pseudolobar in form.

Under the term secondary plague pneumonia are to be included:

(*a*) Pneumonia due to embolic infection of the lungs with plague bacilli in cases of bubonic plague or plague septicæmia.

(*b*) Ordinary bronchopneumonias complicating plague as they do other grave infections—*e. g.*, aspiration pneumonia and the like. The bronchopneumonias of this group are most often due to infection with the streptococcus or the micrococcus lanceolatus. Occasionally an aspiration pneumonia complicating plague is due to the plague bacillus itself. This is particularly apt to occur if there be ulcerated tonsillar buboes.

The only case of primary plague pneumonia recorded in San Francisco occurred before the visit of the Commission. It is Case No. 20 of Dr. Kellogg's series, a Chinese child, aged nine years, who died on November 1, 1900, at 802 Dupont Street.

In some epidemics primary plague pneumonia is the prevailing form of the disease. This appears to have been the case in the Black Death which spread over Europe in the fourteenth century, and also in the Pali-pest in 1836. Plague pneumonia is undoubtedly frequently overlooked during the course of an epidemic.

It is to Childe, of Bombay, that we owe the establishment of primary plague pneumonia as a definite clinical and pathological entity. The patient is taken suddenly ill with a chill, stitch in the side, severe headache, and high fever. The clinical phenomena of a grave pneumonia develop. The respirations are increased from 50 to 80 per minute, and signs of consolidation appear. The pulse is frequent and soon becomes very feeble. An acute splenic tumor can be made out. There may be sensitiveness in the region of the various lymph glands of the body. The typical rusty sputum of ordinary croupous pneumonia is but seldom met with. Instead the sputum is actually bloody (hæmoptysis) and may be copious in amount. There is usually extreme dyspnœa and marked cyanosis.

Nearly all cases of plague pneumonia are fatal, death occurring usually in from one to five days. The duration of the disease may, however, be even longer. During the Black Death it does not appear to have averaged more than two days.

Cutaneous Plague.

Though its existence by some has been denied, it seems clear that *primary* infection of the skin with the plague bacillus is a recognizable form of the disease. The analogy with anthrax here again becomes evident. The cutaneous lesions take the form of vesicles, pustules, or carbuncles.

When the lesions of the skin are secondary they are usually situated over buboes, and the extension to the skin would seem to be directly by way of the lymphatics from the lymph glands. Embolic infections of the skin may be thought of, but from what we know of the cutaneous bloodvessels they are probably rare.

Primary infections of the skin are certainly very unusual, their absence and the absence of lymphangitis between the point of entrance of the bacilli and the first lymph glands to be infected being characteristic features in the majority of the cases of the disease. A judgment as to the primary or secondary nature of a furuncle or carbuncle has to be based upon the time of its appearance. If it is among the first signs to develop, it may be regarded as a primary lesion; if it appear sometime after the onset of the symptoms, it must be looked upon as of secondary occurrence.

Mild Plague or So-called Pestis Minor.

At the beginning and end of large epidemics it is common to find numbers of cases of plague which are so mild that they cause the patients but little inconvenience; probably in many instances mild cases pass unrecognized. The severity of cases in any given epidemic appears to

conform to a curve. The mild cases in the beginning give place gradually to more and more severe infections until at the acme of the epidemic the most violent septicæmic and acutely fatal cases are met with. This stage is followed by a decline in severity until finally the epidemic dies out in a series of mild ambulatory cases. The great importance of these mild cases of plague for the spreading of the disease is obvious. Since the bacilli are given off through the urine and feces an ambulatory case may spread the germs of the disease far and wide. Occasionally an individual who presents what is apparently a mild form of the disease in its early stages may later become very ill. For example, in San Francisco during the visit of the commission one of the fatal cases observed was not considered very ill by his friends in the early part of his attack. Indeed, he walked about and took food with his companions for several days, and it was only shortly before his death that the grave nature of the malady was realized.

There is room for much bacteriological work upon the epidemics of so-called pestis minor. There have been epidemics described in which as many as two hundred cases of the disease have occurred without a death. One naturally asks the question with regard to such epidemics, Are we dealing here with true bubonic plague or with some other disease? Bacteriological examination can alone settle the diagnosis in such instances.

Epidemics of so-called "climatic buboes" have been described by various authors (Ruge, Godding, Skinner, Nagel). The exact nature of these climatic buboes is not clear. While some authorities (Cantlie) assume that the disease is an example of a mild, non-fatal infection with the bacillus pestis, there are others (Godding, Scheube) who are just as positive that the disease is essentially different from plague. Here, again, we are in urgent need of bacteriological study. It alone will settle this mooted question.

In San Francisco, among the physicians who have been in practice there for some time, great stress was laid upon the "glandular swellings" occurring among the Chinese. It was asserted by some of the most experienced physicians in that city that such glandular swellings had been occurring among the Asiatic inhabitants for no less than thirty years. These physicians were convinced that the cases which were proved by bacteriological examination to be plague were precisely the same as those of glandular swelling observed in earlier years. In the absence of pathological and bacteriological examination of cases of so-called "glandular swelling" of the earlier days, it must for the present remain undecided what the nature of those cases really was. Of one thing there can no longer be any doubt—the "glandular swellings" occurring among the Chinese in San Francisco in February, 1901, are instances of true infections with the bacillus of bubonic plague.

In all the infections resembling mild cases of plague the importance of bacteriological and pathological examination for the establishment of the diagnosis is clear. With the help of the naked eye, the microscopical appearance of the lymph glands affected, and of cover-slips, cultures, and animal experiments from the diseased glands, there can be no difficulty whatever nowadays in distinguishing true plague from any other affection.

The Diagnosis of Plague.

In the diagnosis of this disease one will naturally be influenced as to the methods he will pursue by the circumstances under which he is working. If he is to decide as to the nature of the first suspected case in a place where the disease has not hitherto been known to exist, he will be very much more cautious in coming to a conclusion than where he has to pass judgment upon a suspected case in a region in which plague cases are known to be daily occurring. For no conscientious physician will impose upon a community the restrictions as regards travel or the inconveniences and financial loss to commercial interests which the positive diagnosis of plague and the public announcement thereof in a large centre entails unless he is absolutely sure of his ground.

The desirability of coming quickly to an absolutely certain conclusion in a *first* suspected case cannot be too strongly emphasized. It is of the greatest importance if plague is breaking out in a community to establish this fact beyond any possibility of question. Owing to the slowness with which plague tends to spread after its first appearance in a place, it is comparatively easy to stamp it out in the bud or limit the spread to a small focus if the very first case be recognized and the proper measures for the prevention of its spread be undertaken. Then, too, it is only when the people of the community are convinced of the presence of a disease which is capable of giving rise to a grave form of epidemic that they will bestir themselves to employ the proper means for the prevention of its spread and for its utter extermination.

In San Francisco the disease was recognized in March, 1900, and its true nature fully established by competent pathologists and bacteriologists. Whether any or how many cases of plague occurred in San Francisco before this date must remain in doubt. The medical men of the city who had had a training in pathology and bacteriology, or who had learned to have confidence in the results of pathological and bacteriological work, with a few notable exceptions, concurred in the diagnosis and urged the public to take the appropriate measures for the control of the disease. Unfortunately the matter became a political issue. A certain number of medical men, among them several of prominence, denied the existence of plague, and this, together with the

fact that the disease did not spread to any large extent, helped to encourage the public in thinking that the disease was not bubonic plague—a belief which was heartily in accord with their hopes.

A doubt arose in the public mind as to the possibility of making a certain diagnosis in a suspected case. The people were told that no "living case" had been observed, and that the diagnosis rested purely upon pathological and bacteriological examinations. They were further assured that such examinations were insufficient for the making of a diagnosis, and the statement was circulated that bacteriology is "as yet too young a science to interfere in any way with the commerce of a great city."

As a matter of fact, the modern trained physician who has had experience with the disease can make in a case of plague an absolutely positive diagnosis more easily probably than in most of the other infectious diseases. *The diagnosis can be established beyond the shadow of a doubt.* Naturally, when dealing with a first case the most experienced clinician would hesitate to pronounce upon the existence of such a dreaded disease in a community until he had forged a chain of evidence which could not admit of dispute. If he saw the case alive he would subject it to a very thorough clinical examination, would weigh the positive signs with all faithfulness, and would make every effort to exclude the existence of diseases which in any way resemble plague, before deciding that the case was one of pest. If there were buboes, after excluding other possible causes of their origin, he would bacteriologically examine the juices extracted from them by hypodermic syringe. If the patient died he would examine the glands with the naked eye and microscopically, and would make a complete bacteriological examination of these glands, including animal inoculations.

It is not necessary to have a "living case" before one in order to establish the existence of plague in a city. The pathological appearances in themselves are absolutely characteristic in the majority of cases, and the bacteriological examination alone will suffice, if it be positive, for a decision. Fortunate we are that bacteriology, though a young science, has placed in our hands the means of becoming sure whether or not we have among us a disease of such dreadful possibilities as bubonic plague!

It is important, if possible, that men who have had experience with the disease be called upon to give a decision in a suspected outbreak. Aside from the confidence which the public would repose in the diagnosis under such circumstances, it is undoubtedly true that actual first-hand knowledge of the disease, clinically, pathologically, and bacteriologically, goes far to make conclusion in a given case quick and easy. The German Government, recognizing this fact, has arranged for definite plague courses at certain of the bacteriological institutes, where

men may be prepared for the special study of the disease. When a suspected case is reported from any source, plague experts with special plague bacteriological outfits are sent at once to the place, and their report is accepted as final and acted upon immediately.

A large part of the difficulty in San Francisco was due to the non-education of the public and of a portion of the profession with regard to plague matters. As knowledge of plague has increased so rapidly during the past two or three years, and has been so greatly modified during the same period, it is not strange that erroneous views have been and are still in most places prevalent. The idea appears to be very general that if plague once starts in a place it will spread rapidly in the form of a violent epidemic, leading within a very short time to hundreds or even thousands of deaths. Nothing could be further from the truth. It is rare that plague spreads rapidly after the appearance of the first case; it would appear to be only after the rats of the place have become infected that, as a rule, a large outbreak occurs.

The diagnosis in March was made by competent men connected with the City Board of Health and the Marine Hospital Service, and was backed up by the opinion of the professors of pathology and bacteriology in the two best medical schools of San Francisco and by several of the prominent clinicians. The people of the city and State ran a needless risk in not trusting more fully the conclusions arrived at by the scientific men in their midst.

As a matter of fact, nearly all epidemics of plague begin with cases of the bubonic or glandular form, and this is, fortunately, the form which is most easily diagnosed. If one meets with a number of cases with buboes, occurring in the absence of venereal infection, and associated with severe general symptoms, some of the cases terminating fatally, he may, especially if he be dealing with Asiatic peoples, be almost certain that he has to do with an outbreak of bubonic plague. One may now and then meet with a septic case without buboes, but, as far as is known, when septicæmic cases are occurring in a place there are always at the same time other cases with buboes.

In all doubtful cases, and especially where one is dealing with a *first* case, a thorough bacteriological examination should be made. This should include a study of the juice from a bubo, if one be present, the sputum, the blood, the splenic juice, the urine, material from skin lesions, and, should there still be doubt, the feces. Cover-slip preparations, cultures, and animal experiments are to be resorted to. It is Dr. Novy's province to deal with the bacteriological examinations in detail, and I shall, therefore, not enter into the methods here. It is to be remembered that a positive result is of greater significance for diagnosis than a negative one. If no bacilli are obtained from the juice of a suspected bubo one should not stop with the first trial, but should

make repeated examinations until the case is clear. Where the disease is epidemic it is unnecessary, in the majority of instances, for diagnostic purposes to go beyond the cover-slip preparation of the juice of a bubo. If this is positive as regards the presence of the plague bacillus, one need go no further. He who is familiar with the clinical symptoms of plague and with the appearance of the plague bacillus under the microscope, will not require to make cultures or animal experiments if, in connection with suspicious clinical symptoms, he finds great numbers of the characteristic bacilli in his cover-slip preparations made from the juice of a bubo. If there be any difficulty as to the diagnosis, cultures, and especially inoculation of guinea-pigs, will remove all doubt.

The serum reaction in plague would seem to be of but little value for diagnosis except, possibly, to indicate that an individual has had plague at some time previously, for during the first week of the disease, according to Zabolotny, a positive agglutinating reaction is not obtainable. Since in the majority of fatal cases death occurs from the fourth to the sixth day, the uselessness of the reaction for diagnostic purposes is obvious.

Plague may be confused in certain instances with malaria, typhoid fever, relapsing fever, venereal buboes, and other forms of adenitis. Mistakes are not likely to be made, however, if clinicians resort in every case they examine to a thorough routine clinical study of all the features presented. If malaria exists, the parasites should be found in the blood. If the case is one of typhoid fever, in the majority of instances the Widal reaction will be positive. If it is one of relapsing fever, the spirochetæ may be observed microscopically. It is to be remembered that there may be cases of combined infection—malaria with plague, and plague with relapsing fever. The writer was shown such cases in the Arthur Road Hospital in Bombay. In the same hospital, Khan Bahadur Dr. Choksey showed Dr. Flint and myself a form of plague in which there was an associated parotiditis, the plague bacillus probably entering the gland through the ductus parotideus. If there are venereal buboes, the size, resistance, and character of the tenderness of the enlargement will easily distinguish them from those met with in plague, and, further, in most instances, an initial venereal lesion will be discoverable. In all cases, including the various kinds of adenitis, the chief reliance must be placed upon the bacteriological examination of the lymph glands and of the blood from the spleen.

An infection with anthrax might be confounded with the cutaneous form of the plague, but here, again, the bacteriological examination, even of cover-slips, would suffice to differentiate the two diseases.

Plague pneumonia should not be confounded with croupous pneumonia. The sputum is decisive. It consists in plague pneumonia

almost entirely of blood and plague bacilli. Microscopical examination of a cover-slip properly stained in carbol-thionin will reveal typical bipolar staining plague bacilli in enormous numbers. If the plague bacilli are few in number, or are mixed with other bacterial forms so that there is doubt with regard to its presence, a guinea-pig should be inoculated. It is emphasized by Childe that herpes is never present in a plague pneumonia.

If the first case seen is a septicæmic case it is very likely to go unrecognized until after death. The hemorrhages and phenomena of general sepsis in the absence of apparent cause will then excite suspicion, and the bacteriological examination will make the case clear. Nowadays, when cultures from the blood, *intra vitam*, are so often resorted to by clinicians for purposes of diagnosis in cases of general sepsis, we may hope for the discovery of plague septicæmia even *in a first case* during life.

Dengue fever, prevalent in certain districts, might, on account of the general tenderness over the lymph glands, be confounded with plague, but the characteristic exanthem and the mild course of the disease will usually permit one to recognize it even before a bacteriological examination has been undertaken to establish the absence or presence of the plague bacilli.

It must be borne in mind that the peoples among which plague occurs in epidemics live under such conditions that careful clinical and pathological examinations can be made only with considerable difficulty. Practice among the Chinese or among the Hindoos has, perforce, to be carried on in a much less satisfactory way than among Europeans or Americans. Where plague cases are actually known to be occurring in an Asiatic population the only safe method to pursue is to assume every case of fever among the living to be one of infection with plague until it is proved to be something else, and to regard every dead body as a plague cadaver until pathological and bacteriological examinations (including the inoculation of a susceptible animal) have demonstrated the absence of the plague bacillus.

TREATMENT. As to therapy there is but little to be said. The only remedy available in which any confidence is to be placed is the pest-serum of Yersin-Roux. The results obtained with Roux's serum at Oporto were very encouraging. Should the writer develop the disease he would wish to have this serum administered hypodermically in large quantities. Outside of the serum-therapy the treatment is wholly symptomatic.

As a prophylactic measure, Haffkine's inoculation is best for individual protection, though immunity for short periods appears to be afforded by injection of Roux's serum.

THE PATHOLOGY OF BUBONIC PLAGUE.[1]

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My acquaintance with the bubonic plague dates from a visit to Hong Kong, made in the spring of the year 1899 while a member of the Commission sent by the Johns Hopkins University to study the diseases of the Philippine Islands. While engaged in outfitting in Hong Kong opportunity was afforded the Commission, by the courtesy of Dr. Lowson, the civil physician in charge of the Kennedy-town isolation hospital and the mortuary, to inspect those ill of plague and to witness and conduct post-mortem examinations upon those dead of the disease. During this period the several known varieties of the plague were observed. Bacteriological examinations were conducted and a small collection of pathological material made.

No especial use was made of the tissues collected in Hong Kong until recently, when, as a member of the National Commission[2] appointed to investigate the plague in San Francisco, another opportunity was obtained to study the disease and collect a supply of material. The study of this combined material, together with a record of observations upon the general pathology of the disease as presented especially in San Francisco, will form the basis of the present paper.

The epidemic of San Francisco is not traceable directly in a continuous chain of instances to any previous epidemic. The first case discovered in San Francisco, in March, 1900, was accidentally met with, and could not be connected with any previous example or precise infected locality. And yet the fact that the victim was a Chinaman places, with great probability, the source of infection in the Chinese epidemic which has continued without interruption for the past six or seven years.

The Chinese of San Francisco, as of this country generally, are Cantonese, who embark at Hong Kong for America. Although no new importation of Chinese into the United States is known to be taking place at this time, yet the constant travel kept up by those who return for a period to China maintains a continuous communication between our western shores and the southern part of the Chinese Empire. The shipments of food-stuffs, wearing apparel, and objects of art from Hong

[1] Based on remarks made before the Association of American Physicians, Washington, May 1, 1901.

[2] The Commission was authorized by the Secretary of the Treasury, and consisted of Professors L. F. Barker, F. G. Novy, and myself.

Kong to America are constant, and constitute another bond of tangible connection between the two countries.

The first authentic account[1] of the appearance of plague in Europe is the great epidemic known as the Plague of Justinian, which in A.D. 542, starting from Egypt, spread to Europe and all over the Roman Empire, and which, lasting for fifty or sixty years, wrought the most frightful devastation. From that time until 1841, when the plague appeared for the last time in Constantinople, it recurred again and again in different parts of Europe, though latterly only in the southeastern parts of the Continent and in areas becoming gradually more circumscribed. In 1878 and 1879 a small epidemic, which speedily died out, broke out in the Russian province of Astrakan. With the latter exception and the recent limited epidemic in Oporto and Glasgow, Europe has long enjoyed exemption from the plague. America had never been visited until the recent appearance at Santos, Brazil, and the Argentine, and at San Francisco.

The mode of spread to America can best be followed by a consideration of the progress of the recent epidemics in Egypt, India, and China. Egypt, until 1899, had been exempt from plague since 1844, although several epidemics have since the latter date occurred in its neighborhood—in Tripoli (Benghasi), and on the Red Sea coast of Arabia (Assir), from 1853 to the present time. It is said to be endemic in Uganda and the *hinterland* of German East Africa (Koch). Many epidemics have occurred in Mesopotamia, Turkestan, India, China, and Mongolia.

In India there had been several outbreaks during the nineteenth century, but they had been of a localized rather than of a general character. Probably plague is always present in some parts of India, especially among the rude hill peoples. In 1896 it appeared in Bombay, and, possibly, in Calcutta, having been imported to the former city, most likely from Hong Kong.

It is now known that plague has been endemic in the southwest of China, in the province of Yunnan, for many years. It was particularly active in 1871 and 1873, after the great Mohammedan rebellion. From Yunnan, probably following the trade route, it spread to Pakhoi on the Gulf of Tonquin, a severe epidemic occurring in 1883 in that and in neighboring towns. In 1894 it had extended to Canton, where it killed, it is estimated, 60,000 in a population of 1,500,000 (?). Later in the spring of the same year it broke out in the English colony of Hong Kong, subsequently spreading to Macao, Swatow, Amoy, Foochow, Formosa, and probably many other places in the southern

[1] This historical account is abridged and but little altered from the account of Manson, Tropical Diseases, 1900.

provinces of the Chinese Empire. Recently it has broken out in Mauritius, Madagascar, at Delagoa Bay and Cape Town, in South Africa; Osaka and Kobe, in Japan; Manila, in the Philippine Islands; Hawaii, in the Sandwich Islands, and, lastly, as mentioned, at San Francisco, in the United States.

The evidence is complete and incontrovertible that the cause of plague is found in a specific bacillus discovered almost simultaneously by Kitasato and Yersin in the year 1894, during the prevalence of the epidemic in Hong Kong. The bacillus has a characteristic form; it exhibits a marked peculiarity in staining properties; admits easily of cultivation outside the body; readily and quickly undergoes involution upon artificial media, especially when concentrated so as to contain an increased quantity of salts (*e. g.*, chloride of sodium), and also in the tissues after degeneration and after removal from the body or death of the individual, if the examination be delayed for some hours, and is pathogenic for a wide range of animals, causing in them similar symptoms and lesions to those found in the natural infection in man and in the rat. As this paper does not pretend to deal with the purely bacteriological aspect of the plague, a brief reference only will be made to the morphological character of the bacillus.

As seen in recently affected and freshly removed tissues, in secretions or cultures, the bacillus of plague is a short rod, averaging 1.5 to 1.75μ in length and 0.5 to 0.7μ in width. The ends are rounded and the sides convex, the form, therefore, approaching an oval. From the typical form there are two variations: one is shorter and coccoid, the other longer and more definitely rod form. A third variation is ovoid, in which one end appears slightly thicker than the other. All the forms tend to exhibit bipolar staining, the mid-portion remaining unstained or staining more slightly. Complete and uniform staining may, however, be observed. In older pathological processes, and in older artificial cultivations, as well as upon concentrated media, various degenerative forms are found. These consist of oval, ovoid, almost circular, bladder-like, irregularly outlined and even bizarre bodies, which stain with difficulty, slightly, or even not at all, or stain at the margins and not in the interior. A not infrequent degenerative form resembles a dumb-bell or dough-nut (so-called "dough-nuts" of the San Francisco bacteriologists).

Staining is more readily effected in films than in tissues; but in both it proceeds relatively slow. Gram's method is negative. While all the common aniline stains can be employed for staining, the most useful results were obtained with carbol-thionin in weak solutions and after long immersion.

The present description is based upon the study of six cases of plague upon which post-mortem examinations were made. Unfortunately,

with one exception—Case VI.—complete autopsies could not be made. The reasons for this deplorable fact will be found in the succeeding paragraphs, quoted from the official report of the Commission[1] appointed by the Secretary of the Treasury for the investigation of plague in San Francisco:

"In the study of the pathology of cases of plague met with among the Chinese in San Francisco a number of disadvantageous circumstances were contended with. In the first place, owing to the peculiar prejudices of this people—prejudices born especially of their religious beliefs and practices—permission for post-mortem examinations is given with great reluctance. The opposition to all mutilation of the bodies of the dead is so great that consent for necropsies was obtained only after assurance that the examinations would be limited strictly to the actual necessities for the establishment of the diagnosis of the disease.

"In the next place, there is no public mortuary in San Francisco to which the dead bodies were or could be carried. Such examinations as were made were conducted in the narrow limits of a dimly lighted alcove in an undertaker's shop, or in the even worse habitations where the dead were found.

"Under the circumstances the post-mortem examinations left something to be desired on the score of completeness, although in every instance the important question whether death was caused by plague was answered definitely."

The Post-mortem Examinations.[2]

Case I.—Chun Ah Chou, actor, aged forty-four years, died February 5th in Washington Street Theatre. Body well nourished, two or three dark-bluish spots on legs (possibly hemorrhages). On palpation of neck, axillæ, and groins some enlargement of the lymphatic glands of the groin was made out, though nothing corresponding to an outspoken bubo was visible. Incisions were made in each groin, extending from Poupart's ligament about one-third the length of the thigh. The tissues on the left side were swollen and œdematous; the œdema was serohemorrhagic in character, and the lymphatic glands were hemorrhagic and greatly swollen. On the right side the œdema was less marked, and the glands, while distinctly enlarged and reddened, were less altered than those on the left side. Sections of the glands showed them to be uniformly hemorrhagic and swollen, and to contain frequent necroses visible to the naked eye.

The spleen was fully twice the normal size. It was softer than normal, the capsule was wrinkled, and the color deepened.

The examination of films from the glands, periglandular tissues, and spleen showed large numbers of bacilli decolorizing by Gram's method

[1] Report of the Commission appointed by the Secretary of the Treasury for the investigation of plague in San Francisco, under instructions from the Surgeon-General, Marine Hospital Service. Washington, 1901.

[2] Free use has been made of the records of cases in the official report.

and presenting the morphology of B. pestis. Cultures and inoculations of guinea-pigs were also made.

Case II.—Lum Hong Yuen, cook and waiter in Chinese theatre. Illness of three weeks' duration. Said to have quit work on account of chancre and bubo three weeks before death. Four or five weeks prior to death he is said to have had a chill. On inspection of the body no evidence of a chancre could be found. In the inguino-femoral region a large mass of swollen, conglomerated lymphatic glands could be felt. Upon incision of the right groin from Poupart's ligament to the beginning of the middle third of the thigh serohemorrhagic periglandular œdema and uniformly enlarged and reddened glands were found. The amount of fluid was considerable, although there was enlargement of all the glands, some of them reached to the size of a horse-chestnut. On section these were of a deep red color and soft consistence. Necroses were present.

The spleen was enlarged to fully double the normal size; it was softened and of a deep bluish-red color.

Films from the glands and spleen showed large numbers of bacilli having the morphology and staining properties of B. pestis. Cultures and animal inoculations were made.

Case III.—Wong Chi Lui, cigarmaker, aged forty-five years. Illness of two weeks. Complained of fever, loss of appetite, and general uneasiness. There had been pain in the groin and lower abdomen, for which a Chinese doctor had applied a plaster of honey and salve. No history of venereal disease. For three or four days prior to death the man was unconscious. On inspection and palpation a large mass of swollen glands was discovered in the left inguino-femoral region. On incision enlarged glands were revealed about the saphenous opening and in the groin. The largest gland had the size of an English walnut, and was of a dark reddish-brown color; it was soft and juicy in consistence, and mottled with hemorrhages and with grayish-white patches of necroses. The less swollen glands were markedly injected and contained hemorrhages. The periglandular tissue was very œdematous, fluid running freely from the incision.

The spleen was about twice the normal size, soft, and friable.

Films from the glands and spleen showed bacilli presenting all the properties of B. pestis. Cultures and animal inoculations as usual.

Case IV.—Tom Shom, male, aged fifty-one years, actor in Chinese theatre. Had been acting in the theatre two weeks before, although it had been stated that he had not been well for from six to seven months previously. On February 4th he became seriously ill with fever and delirium. There had been some vomiting. On clinical examination, February 8th (Dr. Barker), the patient was found lying upon his back in bed, with legs drawn up. He was in a state of semi-stupor; pulse 108, quick, rather full, but of low tension. The skin was hot and dry. Respiration 20 to the minute. The face had an anxious expression. There was no palpable enlargement of the glands of the neck and axillæ, but in the right groin several enlarged glands could be distinctly felt, and tenderness existed. Died on February 10th. Examination at necropsy showed a slight swelling in the right inguino-femoral region which, on incision, revealed slightly œdematous subcutaneous tissue, with slight enlargement of the glands. The largest gland was the size of a filbert, and its surface was dark and hemorrhagic. On section it

presented distinct hemorrhages. Other glands were swollen, soft, juicy, and hemorrhagic.

The spleen was enlarged, soft, and friable.

Films from the spleen and glands showed large numbers of bacilli having the characteristic properties of B. pestis. Cultures and animal inoculations were made.

Case V.—Ung Ah Buck, aged forty-five years. The day before his death this man was seen alive and examined by Dr. Barker, who diagnosed the case, *intra vitam*, as one of cervical bubonic plague. The patient stated that he had been ill for two weeks. His neck had been swollen for one week, and the condition had been regarded as quinsy. The fauces were swollen and reddened, the swelling being very marked on the left side. The left palatine tonsil was much enlarged, and showed on its surface a grayish-white patch the size of a dime. The reddening of the throat was general, and there was less local injection than one ordinarily sees in diphtheria. On inspection and palpation of the left side of the neck marked bulging was found, due, it seemed, to enlargement of the cervical lymphatic glands. Autopsy: the left side of the face and neck presented a marked diffuse swelling, extending from the angle of the jaw backward to the sternocleidomastoid muscle, and below almost reaching the clavicle.

On incising this region the parotid gland was first reached; this organ presented a normal appearance. After dissecting away the parotid gland a group of greatly enlarged, deep glands, surrounding the carotid artery and jugular vein, came in view. The periglandular tissues were infiltrated with bloody fluid and presented a sodden appearance. The enlarged glands and portions of the surrounding tissue were excised; the former were found to be swollen (several reaching the size of an English walnut) and to be wholly altered in appearance and consistence. In color they were deep purplish, and on incision a hemorrhagic fluid exuded. Opaque points of necrosis were also present.

The general subcutaneous fat was well developed; there was no general œdema. The peritoneum appeared smooth and glistening; there was no fluid in the abdominal cavity, and the abdominal glands were not markedly swollen.

The spleen was enlarged to fully twice its normal size; it presented a purplish color and its consistence was diminished.

The pleural cavities were dry; the lungs retracted moderately upon removal of the sternum; the lower lobes were congested, but no consolidation was made out.

Films, cultures, and animal inoculations were made from the organs and tissues removed at this necropsy, consisting of the enlarged cervical glands and spleen. Cover-slips from the spleen showed large numbers of bacilli having the morphology and staining properties of the B. pestis. The films from the glands differed in their appearance. In some instances there were present large numbers of bacilli similar to those in the spleen, together with a few diplococci or short chains of cocci. Other cover-slips showed, beside the organisms mentioned, a bacillus having the morphology of the B. diphtheriæ.

Case VI.—Foong Ah Fong, female, aged twelve years. No external signs of plague. The spleen only was examined (marked protest from child's relatives). It was enlarged to about twice the normal size, and was diminished in consistence. Films showed a very small number of

bacilli of the size of B. pestis, although the characteristic polar staining was not observed. Cultures were made, and a portion of the spleen was introduced subcutaneously into a guinea-pig, with positive results.

The Histological Examination. The description of the microscopical appearances is based upon the study of the material collected in Hong Kong in 1899 and in San Francisco in 1901. The sections were prepared by Dr. Pearce, to whom my thanks are due. The material covers especially the bubonic cases, hence the descriptions will refer almost exclusively to the changes in the lymph glands and spleen. Tissues from two cases of tonsillar infection (one from Hong Kong) are also available for study. The animal tissues cover a wide range, and include all the organs except the central nervous system. They were obtained from guinea-pigs inoculated with bits of tissues and cultures in San Francisco, and represent the different experimental effects produced by the plague bacilli. Some of the animals succumbed quickly to septicæmic infection, others after many days, in which case pronounced local (bubonic) and visceral lesions were noted; in a few instances the animals were etherized in order to establish the diagnosis or to obtain intermediate effects.

Human Cases. As no histories were obtainable of the cases from which tissues were collected in Hong Kong, and none that were reliable from those in San Francisco, no attempt will be made to consider the disease with respect to its duration; but the degrees of severity of lesions will be described as exhibited by the grade of involvement of the organs studied. The chief distinctions will be afforded by the lymphatic glands, and they will depend upon whether the glands were primarily or secondarily affected. Primary involvement may be of two kinds: Of the first order, being the point of original reception of the virus; of the second order, representing the extension to a second contiguous group of glands. As might be anticipated, buboes of the second order are less marked than those of the first order. Secondary buboes may be found in any or all glands within the body, and at a distance from the primary lesions, infection having followed through the blood circulation. They present, as a rule, an example of involvement of least intensity.

Lymphatic Glands—Primary Buboes of Second Order. These glands show to the naked eye slight swelling and congestion. Upon microscopical examination, in the least marked cases, the changes affect especially the lymph sinuses. As might be anticipated, the subcapsular sinuses show very early involvement. Even when the medullary sinuses show very slight alterations the cortical sinus is dilated and contains numerous large cells, with round nuclei and finely granular and vacuolated protoplasm. These large cells quite completely fill the sinus. When the subcapsular space exhibits this condition, and it is present in glands that are regarded as scarcely enlarged, similar cells are to be

found about the main trabeculæ in the interior (medulla) of the gland. That they are the cells that later show marked phagocytic properties for red blood-corpuscles is certain. In this early stage the lymph nodes and cords are little affected. There may be some increase in the lymphoid cells about the larger veins, but no very marked alterations have, as yet, taken place. There is complete absence of necrosis. Throughout the gland fine strands of fibrin can be seen, indicating doubtless an inflammatory (?) œdema. The bloodvessels contain light, fibrinous, possibly agonal or post-mortem thrombi. At a later stage, when the glands are definitely although not greatly enlarged, the changes are more diffuse and more profound. All the sinuses are much enlarged ; the cellular proliferation within the sinuses is also a marked feature, and the new cells are highly phagocytic exclusively for red blood-corpuscles. These cells cannot be distinguished from the red blood-corpuscle carrying cells of the spleen in typhoid fever. The lymphoid cells proper are also increased, beside which the centres of the lymph nodes and cords show a great increase in swollen and pale cells, their centres being converted into pale areas composed of cells of the epithelioid type. A small number of nuclear fragments also occur in these areas and chiefly within cellular protoplasm. The foci described are similar to those found in lymph glands and the spleen in other infections or toxic diseases—*e. g.*, diphtheria and typhoid fever.

The bloodvessels in the early stages of swelling contain an increased number of mononuclear and polymorphonuclear white cells. As the intensity of the process grows, their number increases. With the progress of the swelling, etc., the number of vascular thrombi increases and their nature changes. They appear in large vessels and contain many more white cells.

The relation of plague bacillus to these buboes is perhaps variable. What I should take to be the normal is a small growth, especially in the blood and lymph vessels, the bacilli demonstrable among the lymphoid cells being fewer. The bacilli exist free among blood-corpuscles and other cells. On the other hand, I have seen in buboes of the second order a growth of bacilli as great as in those of the first order. What is, however, very striking in these instances is the absence of anything like an adequate reaction on the part of the gland; and, moreover, the existence with as little reaction of equally large masses of characteristic bacilli in the periglandular adipose and other tissues. I am, therefore, inclined to view this abundant growth either as being agonal, or, what I think even more probable, as of post-mortem development.

Primary Buboes of the First Order. The pathological changes in these glands are unmistakable. They exceed in intensity and in extent those of the preceding order. They, moreover, differ in kind, first, on account of the occurrence of hemorrhage, and, second, on account of the necrosis. The two sets of lesions can be compared with difficulty on account of the degree to which the structure is lost by necrosis, etc., in the glands now being considered. Again, while the periglandular affection in the former order was slight, the outline of each gland being defined by its capsule, in the present one such sharp limits are entirely missing; the periglandular involvement is as great as the glandular affection, and the necrosis, hemorrhage, etc., are as marked. On account of the nature of the interglandular tissue, the presence of large

blood and lymph vessels, nerves, etc., the histological appearances differ from those of the glands themselves.

In all the specimens of glands which I have examined no separation into the medulla and cortex is possible. Masses of lymphoid cells still remain, but they do not compose typical structures. That they are the relics of cortical structures their position proves; but they are not in relation with a definite systematic arrangement. The medulla is even more altered in that all the proper cells are necrotic. Only fragments remain of the large, swollen, phagocytic cells, and the intercellular stroma stains poorly or not at all. What can be made out clearly are granular material, containing remains of cell-forms, nuclear fragments in small numbers, shadows of red corpuscles, and plugs of finely granular structure, filling spaces which suggest pre-formed vessels, and which, from the regularity of the grains, can be recognized in the hæmatoxylin specimens to be bacilli. This granular and amorphous detritus is continuous with similar material in the cortex, only that in the latter situation small foci and islands of lymph cells still persist. This same regular, granular appearance mentioned proves that many bacilli occur throughout this entire area. Hemorrhages also exist in the cortical parts.

The bloodvessels commonly are thrombosed. The thrombi consist of cells, both mononuclear and polymorphonuclear, and fibrin. The walls of the smaller vessels often are hyaline and structureless. Specimens stained with the fibrin stain show a fine network about the vascular walls, occurring partly within the lumen, partly within the wall, and partly beyond in the perivascular tissues. Larger vessels show, instead of the fibrinoid transformation of their walls, destructive and infiltrative changes. The intimal and medial coats contain an increase of cells and many cell fragments. This infiltrative condition is especially marked in the middle coat. That many of these cells are polymorphonuclear blood cells is shown by the bizarre forms, etc., and the staining properties.

The periglandular structures are extensively infiltrated and usually show necrosis as well. The infiltration is partly cellular, partly fluid, along with which fibrin is perhaps invariably present. The cells consist of red corpuscles and small elements with single, deeply-staining, much fragmented, or polyform nuclei. The œdema and fibrin are found chiefly in the coarse, fibrous septa of the adipose tissue; the cells occupy the meshes of the fat cells. The necrosis may be microscopical in extent, affecting a small number of cells, or large areas may be without definite structure and present a granular appearance. The bloodvessels are frequently thrombosed, and their walls inflamed (as above).

The nerves are involved in the exudation. The cellular infiltration is found only in the perineurium, but this may be invaded to such an extent as to present the appearances of a small-celled collar surrounding the nerve bundles. The bloodvessels within the nerves are dilated; the nerves (in alcohol preparation) appear swollen, and the cells of the endoneurium are occasionally fragmented. Vessels with thin walls, presumably lymphatics, contain formless plugs in which there are many bodies taken to be bacilli.

Bacilli are abundant within the swollen glands and in the periglandular tissues. Sections stained in thionin show countless numbers. In

no known bacterial infectious process, not even in leprosy, are such large numbers of bacteria to be found. They occur in continuous growth throughout the glands, occupying every available space; they completely occlude many bloodvessels, or, mixed with definite thrombi, compose a considerable part of the plugs. Moreover, the walls of the bloodvessels contain masses of bacilli, having grown, it is safe to conclude, within the vasa vasorum and the lymph spaces. The adventitial coats of veins and arteries are especially rich in such growths of bacilli. The bloodvessels and lymph vessels in the periglandular structures are also, to a large extent, occupied by bacilli. The latter seem to be plugged by these growths alone; the former may show bacterial masses, even when the vessel is still open and pervious. Large areas of finely granular detritus in the interstitial tissue are made up of a massive growth of bacilli; and the bacilli occur in the fluid exudate. The morphology of the organisms speaks unmistakably for the bacillus pestis.

The Tonsillar Infections. The buccal mucous membrane forms one of the portals of entry into the body of the plague bacilli. It is probable that the cervical buboes arise from that source of infection. Of all the buccal structures the tonsils seem to be most frequently the primary one attacked. In this fact we have only another illustration of the importance of incomplete epithelial investment and perhaps of previous disease in promoting infection. Other parts of the buccal cavity may become secondary points of development of the bacilli, an example of which is supplied by a case from which tissue was obtained in Hong Kong, and which shows early involvement of the epiglottis.

The tonsil suffers changes not unlike those described in the primary lymphatic bubo of the first order. There is congestion, hemorrhage, necrosis of cells, and extensive growth of bacilli. The degrees vary somewhat, so that examples of lymph sinus proliferation may be met with along with other changes of greater severity. The cells of the sinuses are somewhat smaller than in the lymphatic buboes; some resemble Unna's plasma cells closely, *and many are phagocytic for bacilli.* Of this there can be no doubt, for the protoplasm of these cells is packed with characteristic organisms. The bacilli are spread beneath the layer of stratified epithelium, even elevating this layer through the excessive growth, the epithelium showing vacuolation, loss of nuclei, etc.

The lesion of the mucous membrane covering the epiglottis is more recent than in the tonsil. It consists of a marked infiltration of small cells with single nuclei, polymorphonuclear cells, and serum. The infiltration extends to the layer of mucous glands next the cartilage, which are in part broken up by it. The chief growth of bacilli is near the surface, beneath the epithelium, which layer, it should be mentioned, is in part deficient. Occasional masses of bacilli occur in the deeper layers and even within the lumen of the glands. The appearances here presented are not unlike those described of the primary plague pustule.

The adjacent glands suffer along with the tonsils; their enlargement constitutes, of course, the cervical bubo. Two kinds of glands must, however, be distinguished in this region—lymphatic and hæmolymphatic glands. The former undergo the changes already described. In addition, it should be mentioned that even with considerable enlargement the alterations noted in one gland—the one constituting the main bubo—resemble closely those of the glands of the second order, except for

greater richness in bacilli pestis. The lymph sinuses especially were affected; the cells were increased in numbers, enlarged, plasma-cell forms occurred, but phagocytosis was for bacilli only. The lymph node and cord cells were also increased, but not degenerated. Occasional mitoses were met with in larger (endothelial) cells.

The *hæmolymph* glands were greatly enlarged; the network of vessels enormously distended; much hemorrhage had taken place; nuclear fragments were scattered numerously throughout the tissue; a small number only of cells with undegenerated nuclei were still present; the periglandular tissue was hemorrhagic, and micro-organisms—bacilli—were abundantly present. In Case VI. of the San Francisco series the very hemorrhagic glands described consisted of these structures.

The Spleen. As already described, the spleen in the plague is enlarged moderately; the consistence is somewhat diminished, and the color deeper than normal, but it is not the type of the acute splenic tumor of the true septicæmias. In making this statement it is well to emphasize that although the spleen in the autopsies made all contained bacilli, often in very large numbers, the cases themselves were examples of the bubonic and not of the septicæmic variety, *per se*, of the disease. In a case of pneumonic plague which I saw with Lowson at Hong Kong the spleen was much swollen (three to four times the normal size), and very soft and dark.

It is probable that, irrespective of their mode of origin, all fatal cases of the plague are septicæmic (bacteriæmias). But it is also probable that the general invasion of the bacilli takes place late in many bubonic examples, and the enlargement of the spleen is, therefore, less marked a feature than in the primary septicæmias, or even the pneumonic variety, in which dissemination of the organisms occurs earlier in the course of the disease.

The microscopical changes vary in different cases, but in degree only, so far as can be determined by the study of bubonic cases. The alterations affect the pulp chiefly, next the lymph nodes (Malpighian bodies), and then the bloodvessels and stroma.

The pulp is swollen, the swelling being the result of cellular proliferation, cellular infiltration, and œdema. The proliferation affects especially cells closely united with the veins and surrounding the trabeculæ. These cells have reticulated nuclei, placed eccentrically, and a fair allotment of protoplasm taking the blue thionin stain. The cells are often polyhedrical rather than round. These cells have a close affinity to Unna's plasma cells. Next the lymphoid cells are increased, but to a less extent than the cells just described. The vascular and other (?) spaces in the pulp contain an increased number of red corpuscles. In the same spaces occur large cells of two kinds. One is a giant cell with single, lightly-staining, reticulated nucleus and a moderate amount of protoplasm, and resembling the large, mononuclear, narrow cell with which it is probably identical; it is not phagocytic. The other is a much larger cell, three to four times as large as the narrow cell, and is highly phagocytic. These macrophages englobe white cells—both mononuclear and polymorphonuclear—but rarely red corpuscles. They occur at times within the larger veins, especially such as exhibit the subintimal cellular proliferation to be described. The polymorphonuclear cells in the pulp exhibit great variation in

form, and many would seem to have been in a state of active migration when the tissue was fixed. They show great variety of form, such as is seen in actively motile cells, and they would seem to be moving in numbers through the pulp. Fibrin, in the form of balls and fine strands, is found among the pulp cells and in the fluid, and many bacilli are present.

The Malpighian bodies are increased in size, the increase being due to the multiplication of the lymphoid cells, and, to a smaller extent, of epithelioid cells. The latter do not occupy the centres of the nodes, but are few in number and placed peripherally. Their nuclei are large and vesicular; rarely a cell contains two nuclei. Degeneration of cells is uncommon, very few fragmented ones being visible. Rarely small islands of fibrin are present in the nodules.

The bloodvessels show two kinds of change. The arteries, chiefly those of the Malpighian bodies, have hyaline walls; the veins of all sizes frequently show subintimal cellular proliferation. The cells in the intima are mononuclear and more rarely polymorphonuclear elements that form a continuous although not uniform investment, or appear as isolated projections into the lumen of the vessel. Above these cells the displaced endothelial cells can usually be detected.[1]

Bacilli are very numerous, especially in the pulp, where they grow diffusely and would seem to attach themselves to the reticulum and grow in irregular masses into the venous sinuses. They are rarely within cells. Their morphology is unmistakably that of B. pestis. They also completely occlude small bloodvessels, and, within the trabeculæ spaces, probably lymphatics. In that the richest growths are often unassociated with reactions, it is highly probable that they may have taken place post-mortem.

So few specimens of the remaining organs could be collected that no description of them will be attempted.

The Experimental Disease—Morbid Anatomy. As stated at the outset, the animal used for experiment was the guinea-pig. The inoculated material consisted of bits of spleen and lymph gland and cultures, upon agar, from those sources. The place of inoculation was the subcutaneous tissue of the lateral abdominal wall, nearer the inguinal than the axillary region.

The inoculated animals[2] can be separated into two groups, depending upon the results of the inoculation. These results in turn depended upon the virulence of the material—tissue or culture—inoculated, upon which also depended the duration of life following inoculation.

Types of Infection. The animals inoculated early in the course of the investigations in San Francisco died at periods varying from forty hours to eight days. Those inoculated later, and one or two inoculated with cultures early in the studies, but which had not succumbed, were etherized at the close of the work and subjected to post-mortem examination. According to the period of survival and virulence of the inoculated material, the appearances observed denoted (*a*) bacteriæmia without macroscopical localization in the organs, and (*b*) focal, nodular

[1] This process is identical with that described by Hektoen in tubercular meningitis; Councilman in epidemic cerebro-spinal meningitis; Pearce in the spleen in scarlet fever; and Flexner in the lung in experimental leptothrix filiformic pneumonia in the rabbit.

[2] See Report of the Commission, p. 17 et seq.

localizations in the internal organs. In all cases marked local lesions at the site of inoculation and in the adjoining tissues occurred.

Local Lesions. At the point of inoculation the tissues—skin, subcutaneum and sometimes muscles—were infiltrated with pus cells and presented a yellowish focus of necrosis. From this area as a centre the subcutaneous tissue, sometimes of one side, but frequently of both sides, was occupied by a gelatinous, hemorrhagic infiltration.

The lymphatic glands of the inguinal and axillary regions, even in the acute cases, were distinctly enlarged. In those animals which died after a longer period, or were killed from six to seven days after inoculation, the regional lymphatic glands were much enlarged, hemorrhagic, and even necrotic. The inguinal glands were, as a rule, more swollen than the axillary.

The Spleen and Liver. In the instances of rapid death (bacteriæmia) the spleen was moderately enlarged, its color was deepened, its consistence decreased, but no focal lesions were visible to the naked eye. In this class of cases the other organs failed to show focal lesions. The lungs appeared mottled only, and a few small necroses existed in the liver; numbers of bacilli were contained in all the viscera and in the heart's blood.

The focal lesions in the spleen consist of grayish-white nodules, larger than a millet-seed in size, covering the surface (within the capsule), and occupying the substance of the organ. When the nodules are numerous—*e. g.*, in animals succumbing from the sixth to the eighth day, or after etherization at that period, when there has been a marked local reaction—the spleen is greatly enlarged, perhaps five to six times its normal size, and its color is pale. The main mass is composed of the nodules now almost or actually confluent which, having penetrated the peritoneal capsule, are covered on the surface with a fibrinous exudation.

The liver invariably shows lesions when death has been delayed a few days. The common ones are focal necroses of varying size. These are yellow in color, and in size ranged from that of a pin's point to linear and wedge-shaped areas three to four millimetres in length. Only rarely did whitish nodules similar to but smaller than those noted in the spleen occur.

The Lungs. They present a variety of appearances, only one of which was characteristic. Sometimes they showed no gross lesions; not uncommonly they are mottled and contain small ecchymoses beneath the pleura; rarely they contain scattered whitish nodules resembling those of the spleen, except that they are smaller and tend to be surrounded by a zone of recent hemorrhage. No effusions into the pleura were noted.

Subserous Hemorrhages. These are common, especially in the peritoneum, where they occur beneath and within the serosa of the large intestine, and in the pleura covering the lungs. They are usually small in size, although at times, through confluence, they reach larger dimensions. However, considerable exudations or effusions into the serous cavities did not arise from this source.

The other organs, except the adrenal glands, showed no special changes to the naked eye. The adrenals were uniformly congested, and often very dark in color.

The central nervous system was not examined.

Histological Examination[1]—*Local Lesions.* This embraces (1) the site of inoculation, and (2) the adjacent lymphatic glands. 1. Upon microscopical examination it is found that the abdominal muscles are involved in the local infection. The lesion consists of necrosis, extensive infiltration, and proliferation of the local tissues. The infiltration exceeds the necrosis, but the proliferative changes are considerable. The necrotic tissue is infiltrated with cells containing polyform and fragmented nuclei, many staining very poorly. Among these a fair number of cells with single vesicular nuclei are also found, they probably arising from the fixed tissues. The cellular and necrotic mass is surrounded by voluntary muscle, fibrous, and adipose tissue. Remains of these several tissues may also be found in the phlegmon, especially fragments of muscle; but the adjacent muscle fibres are swollen, sometimes fragmented, and if the phlegmon is large much compressed and elongated. But the main change is found in connection with the sarcolemma, which is in active proliferation, separating widely the remaining fibres in the older specimens, and giving rise to a marked interstitial myositis. The adipose and connective tissues are also in active proliferation. Newly-formed bloodvessels are numerous, and the phlegmon is enclosed by the new tissue.

Notwithstanding the evidences of healing and the marked reaction, the number of bacilli present is very great. They appear in large clumps and in the form of a diffuse growth, not only in the phlegmon, but also in the adjacent newly-formed tissue, and are largely without cells.

2. The lymphatic glands show degrees of swelling, etc., in part according to their positions, and depending upon their mode of infection. Division into primary buboes of the first and second order is also justifiable in animals. The main lesions consist of hyperæmia, cellular proliferation, exudation, and bacterial growth. The cellular proliferation and bacterial development predominate. The former is met with in the medulla and the cortex, and affects lymphoid cells (in the cortex especially), and a larger cell with eccentric nucleus and more abundant, deeply-staining protoplasm (chiefly in the medulla). The larger glands (primary buboes of first order) show much necrosis, the cells being extensively fragmented. In these, moreover, fibrin is present, both as fine fibrils throughout the gland and in the form of more compact masses within the vessels. As many of the plugged vessels are in the medulla, occupy the position of the lymph sinuses, and are devoid of red corpuscles, they are taken to be lymphatic vessels. The periglandular tissues are invaded also. Infiltrations, exudations, and necroses are met with in the cellular and adipose tissue; bacteria are also numerous. The bacilli in the main buboes are as numerous as in cases of human infection, and have much the same distribution. An exception is found in the less conspicuous involvement of bloodvessels in the experimental buboes.

The Spleen. There is little similarity in this organ in the human and experimental disease. The sole diffuse change in the latter is congestion, which is often so marked a feature as to cause wide dilatation and make very conspicuous the blood sinuses of the pulp. The white cells also are increased, and especially a large mononuclear cell. The

[1] The histology of experimental plague lesions has received relatively little attention. The main description, with the facts of which the above is in considerable agreement, is given by Babes and Livadite in Virchow's Archiv, 1897, Bd. cl. p. 343.

Malpighian bodies are but little altered. Unless there have been nodular formation in the spleen little else is found except bacilli, which may be abundant, especially in the pulp.

The localized nodules are what constitute the characteristic lesion. They consist of a central body of bacilli about which are grouped cells and remains of cells, forming collections as large as or larger than the Malpighian bodies. The bacilli may form a central mass with radii projecting from the periphery, or the development may have taken place from several centres, the latter being united by intervening strands. The cells surrounding the bacilli are in part mononuclear elements, having vesicular nuclei; but in the main they are polymorphonuclear, fragmented, and degenerated cells. In one specimen, areas composed only of mononuclear cells, but with slight bacterial development only, were observed. Fibrin is present about the areas, within the vessels, and in the tissues. The quantity of fibrin varies in the different specimens.

From the position of the bacilli it would appear that they developed in bloodvessels, which finally became occluded. Following this cellular proliferation doubtless took place, although previous degeneration of splenic tissue may have occurred. The degeneration of the new cells seems to have provoked a rich emigration of leucocytes toward the areas of bacterial development. The bacteria are free, without cells. In addition to the masses (emboli?) of bacilli a general diffuse growth of organisms is also present in the splenic tissue.

The Liver. The focal lesions of this organ consist, beside rare hemorrhages, of necroses and nodular formations not unlike those found in the spleen. Of the hemorrhages, which do not reach a large size, it is unnecessary to speak further; the necroses are, however, important. The latter are separable into two groups: those attended and those unattended by proliferative phenomena. Together they constitute the necroses described as visible on the surface of the organ as dots and lines. Similar ones may be present also in the depth, and in both the liver cells are found in various stages of hyaline or coagulative necrosis. The protoplasm is highly refractive, shows an increased affinity for eosin, the nuclei of the cells may be absent, in a state of pyknosis, or fragmented. Remains of previous vacuolization or fatty change may be discovered in the liver cells. A small number of leucocytes may occupy the capillaries between the cells. Bacilli are sometimes demonstrable in the sections among the hyaline cells, sometimes not. They doubtless are always present, but not clearly stainable. Thrombi are usually absent.

A more characteristic lesion is found in the nodules with which necroses of liver cells are usually associated. The nodules vary in number, position, and size in different specimens. In some instances they were entirely absent, although the simple necroses existed. They are associated, perhaps invariably, with considerable growths of bacilli, forming zooglea masses, which occupy the centres of the nodules. About these there is a rich cellular accumulation, which I take from the study of many sections to arise as follows: The bacilli having localized within the liver, a multiplication of the endothelial cells of the neighboring capillaries takes place. As these cells—presenting epithelioid appearances—increase the adjacent liver cells also begin to show alterations, among which are swelling and vacuolization of proto-

plasm, multiplication of nuclei, compression of protoplasm, and hyaline degeneration. A little later stage exhibits the disappearance of many of the liver cells, their place having been occupied by the epithelioid cells, so that the new formations at this time look not unlike miliary tubercles. One difference is, of course, immediately noticeable, the bacilli being numerous and easily demonstrable. Another difference is found in the tendency of the node to enlarge by exciting the adjacent structures to similar proliferative activity. Finally, the large size of the nodules and the extent and irregular distribution of the liver necroses constitute marked differences from the appearances seen in tuberculosis. Moreover, there is no caseation in the nodules, or any process to be confounded with it, although disintegration by fragmentation of cells commences very soon. About this time polyform cells, probably polymorphonuclear leucocytes, make their appearance and mingle with the other cells. In the oldest nodules nothing remains of unaltered or only slightly changed liver cells in the centres of the formations.

The nodules may occur anywhere within the liver lobule and in the interlobular tissues. Thrombi, hyaline and fibrinous, may be present in the adjacent veins and capillaries. The cellular proliferation and infiltration, instead of giving rise to a definite node, may extend in a linear direction along the walls of bloodvessels or bile vessels. In the former the endothelial lining of the vessels tends to increase. In one specimen a considerable linear envelopment was noticed along one side of a medium-sized branch of the hepatic vein.

The effects of the presence of the bacillus pestis in the liver of guinea-pigs is to cause general and local degenerations, and, by their occurrence in large numbers, to excite circumscribed proliferation of the endothelial cells and perhaps, although only to degenerate quickly, the liver cells. The lesion which results from the latter process is the characteristic plague lesion in the liver, and corresponds more or less accurately with the focal lesions in the spleen. It is the result of the direct action of the bacilli or their metabolic products *in situ*. The more remote effects of the bacilli are degenerative only.

The Lungs. Subpleural and intrapulmonary ecchymoses are not uncommon. The characteristic lesion is, however, focal and nodular. In number, size, and distribution these nodules are subject to great variation. They may be absent altogether, very few may be present, or every section of the lungs may contain a dozen or more. They may be near or within the pleura, in the substance of the lungs, or adjacent to bronchi. In size they vary from the area of two or three to areas of twelve or more pulmonary alveoli. Bacilli in masses are always present. They are within the alveolar spaces and in the pulmonary capillaries. About these are cells, the major being within the alveoli, and consisting of or resembling the alveolar epithelium. Cells with polyform nuclei and cell fragments are intermingled. The stroma is also infiltrated with similar cells. The larger the nodules the more irregular in form the cells, and the greater the number of fragments. Beside the bacilli within the nodules a growth may also have taken place in pulmonary capillaries, about which there may have been no considerable cellular accumulation.

The adrenal gland shows extensive hemorrhage, marked especially within the medulla, the structure of which is greatly disturbed. The cortex, on the other hand, exhibits an extensive growth of bacilli, which

run between and surround the cortical cells and occupy spaces beneath the capsule of the gland. Isolated masses of bacilli are also present in the medulla.

The present epidemic of plague in China and India has been noteworthy, first, because of the discovery of the specific cause, and, second, as permitting accurate studies of the varieties, modes of infection, prophylaxis and specific treatment of the disease. A host of contributions to our knowledge of the plague have been made by private individuals and Commissions sent to the East by Japan and several European countries. Brief reference will be made in this place to the pathology of the disease, as described in some of the published reports, in order that comparison may be made with the San Francisco epidemic which supplied the chief materials for the present paper.

According to the German Commission[1] the pest bacilli find their way into the body either through wounds of the skin or by way of the lungs. The first mode of infection gives rise to the great majority of the cases. It is presumed that minute lesions—scratch wounds, etc.—open the way. No unmistakable example of intestinal infection was observed, while, on the other hand, instances of infection starting from the tonsils or other parts of the buccal mucous membrane were encountered. In a considerable proportion of cases pustules or carbuncles of the skin, representing the primary points of entrance, from which the regional lymph glands became affected with bacilli, were noted, and between the two stations distinct lymphangitis is said to have occurred. Bubonic plague may eventuate in absorption, in suppuration, or it may be associated with severe symptoms denoting spread of the infection or a general intoxication of the organism. The hemorrhages which are present in various parts are due to intoxication, in support of which conclusion an instance of the examination of a fœtus expelled on the third day of the disease is cited. In it typical hemorrhages were present, but no bacilli whatever could be demonstrated in cultures, etc. Bacilli were not, moreover, obtainable from petechial blood. The commission also recognized a severer form of the plague—the pest septicæmia—and in addition a primary plague pneumonia that may be mistaken for croupous pneumonia.

The report of the Austrian Commission[2] differs in some respects from

[1] Mittheilungen der Deutsch. Pest-commission aus Bombay, etc., Deutsch. med. Wochenschr. Sonderbeilage zu No. 17, 1897; Weitere Mittheilungen der Deutsch. Pest-commission, ibid., Nos. 19, 31, 32, 1897; Gaffky, R. Pfeiffer, Sticker, und Dieudonné: Bericht über die Thätigkeit der zur Erforschung der Pest in Jahre 1897 nach Indien entsandten Commission, Arbeiten a. d. Kaiserl. Gesundheitsamte, 1899, Bd. xvi..

[2] Zusammenfassender Bericht über die Thätigkeit der von der Kaiserlichen Akademie der Wissenschaften in Wien zum Studium der Pest nach Bombay entsendeten Commission (Wiener klin. Wochenschr., No. 20, 1897; Müller, Albrecht und Ghon, Ueber die Buelenpest in Bombay in Jahre, 1897. Gesammtbericht der von der Kaiserl. Akademie der Wissenschaften in Wien zum Studium der Buelenpest nach Indien entsendeten Commission. Theil 1 und 2, A und B, Wien, 1898-99).

the German, and it is important as containing extensive descriptions of the gross and microscopical appearances of the organs in the plague. The report was based upon the clinical observation of seventy cases of plague and the bacteriological and pathological examination of forty-seven cases. The chief form of plague is denominated by them "septicæmic hemorrhagic." It is characterized by a primary hemorrhagic bubo located most frequently in the inguinal, axillary, and cervical regions, about which there occurs a hemorrhagic œdema, and at a greater distance hemorrhages into the organs. The spleen is swollen, the general lymph glands are enlarged, and the parenchymatous organs show degenerative changes. The primary bubo may be entirely wanting, the swelling of the lymph glands may be inconspicuous, and the hemorrhage may be the only pronounced sign. A second form of the pest is the septicopyæmic. In it embolic foci are present in the lungs, liver, and kidneys. A third form is the primary pest pneumonia, which is a confluent lobular pneumonic process, usually attended with noticeable lymphatic enlargement. The common place of entry of the bacilli is the skin, but only exceptionally can the precise point of entrance be discovered, the demonstration of the place and mode being found in the location of the primary bubo. The lymphangitis in the neighborhood of the buboes as well as the infiltration of the periglandular tissue are always secondary to the glandular infection. A tonsillar infection is described, and the lungs are admitted to act as the portal of entry for the bacilli in a small number of cases. A single instance of purulent meningitis, due to the bacillus pestis, was encountered. Clinically, there should be distinguished only bubonic and pneumonic forms of the plague. The former is much the more frequent. In all but a very small number of cases the primary morbid focus is found in a lymph gland or a group of glands (primary bubo) from which, through lymphatic communication, the adjacent glands become infected. The latter constitute the primary bubo of the second order, in contradistinction to secondary buboes, the result of general invasion of the body by the bacilli. The invasion of the blood takes place always from the primary bubo (or lung), as a primary blood infection does not exist. The primary bubo may be so small that it cannot be discovered clinically, and is found anatomically only after careful and prolonged search. In *foudroyante* cases it may fail altogether.

The primary bubo is distinguished by destruction of the lymphatic parenchyma, necroses, hemorrhages, and (in the cases of mixed pyogenic infections) suppuration. A similar condition is found in the surrounding cellular tissues. Bacilli are present in great numbers. The secondary buboes show, on the other hand, uniform hyperæmia, occasional hemorrhages, and, in the more protracted cases, medullary swelling. The primary buboes of the second order approach one or the other

of these appearances, depending upon their distance from the gland primarily affected.

The multiple hemorrhages are not the results of the action of toxins elaborated at a distance, but are caused directly by the bacilli which may always be found in the neighborhood.

Parenchymatous and fatty degenerations of the heart, liver, and kidneys occur commonly. Splenic tumor is a constant occurrence. The spleen shows marked changes. The pulp is distended with blood, and contains many polymorphonuclear cells. The follicles are but little altered, but the trabeculæ are swollen and homogeneous. In some instances the endothelial cells of the pulp have proliferated and desquamated. When very great numbers of bacilli are present miliary necroses may occur (also oberved by Yamagiwa).[1] The bacilli may be very abundant in the pulp, but are spare in the follicles. They are sometimes contained within cells.

In the pyæmic variety metastatic foci are found in the liver, lungs, kidneys, spleen, and musculature. These foci, which may reach a hazel-nut in size, resemble abscesses, except that they tend to be surrounded by a zone of hemorrhage. In about one-third of all the cases of plague secondary pyococcal infection has taken place.

The primary plague pneumonia appears in the form of a lobular consolidation, which, when the foci are numerous and confluent, may produce lobar solidification. Bronchitis is present. The bronchial lymphatic glands present appearances of primary, the other glands of secondary buboes. In addition to the primary two other forms of pest pneumonia are recognized; one metastatic, which appears as multiple and larger foci, seated beneath the pleura; the other an aspiration pneumonia, from inspirations of infected material obtained from buccal buboes.

Wyssokowitz and Zabolotny,[2] who were sent by the Russian Government to Bombay, performed autopsies upon twenty-four plague cadavers. They recognized two modes of infection—from wounds and through the lungs. In the former cases lymphangitis was usually missed, so that the exact place of entrance could not always be given; on the other hand, the territory of infection could be determined by consideration of the glands primarily involved. In their series of pneumonic cases (six) all were examples of bronchopneumonia. In no instance was a gastro-intestinal source of the infection noted. While the mesenteric glands were swollen they did not present the appearances of primary buboes.

Wilm[3] examined a large number of pest cadavers in Hong Kong.

[1] Ueber die Bubonen-pest, Virchow's Archiv, 1897, Bd. clix. p. 159, supplement.

[2] Recherches sur la peste bubonique, Annales de l'Inst. Pasteur, 1897, t. xi, No. 8.

[3] Ueber die Pest-epidemie in Hong Kong in Jahre 1896, Hygienische Rundschau, 1887, Bd. vii., Nos. 5 and 6.

Especial attention is drawn to the involvement of the gastro-intestinal tract. The solitary and agminated intestinal lymphoid nodules were generally swollen and hemorrhagic, and the mesenteric glands were found swollen, softened, and mottled with hemorrhages. Wilm claims to have found in 20 per cent. of the cases without external buboes that the stomach and intestine were predominatingly affected. This observation thus far stands alone and in opposition to the experiences of other writers.

The two main types of the plague—the bubonic and pneumonic—may be considered as established by the observations made during the present epidemic. Additional confirmation of the studies in China and Hong Kong have recently come from Japan[1] and Sydney, N. S. W.[2] Viewed by the light of the experiences in other places where the plague has gained even a temporary foothold, the absence of the pneumonic disease from San Francisco is the more remarkable. In all places where plague has secured a start evidences of rat infection and probable rat dissemination have been brought forward. It is, therefore, the more strange that in San Francisco, even after a year's prevalence among the Chinese, no evidence of a similar infection of vermin has been obtained. An attempt was made by the National Commission to determine whether the rats in Chinatown harbored the plague. Only one dead rat was obtained for examination, and it proved negative. This animal showed signs of traumatism about the body, and may have been killed by a dog or by other violence. About one dozen rats were caught in traps in the sewers in the Chinese quarters. They were fed and kept under observation for about two weeks, during which time only one died. Upon examination this animal gave a negative anatomical and bacteriological result. The others were killed but not examined.

It is, therefore, safe to assume that no considerable if any spread of the plague due to the rats in Chinatown has taken place. And it seems not unjustifiable, judging from the experiences of other infected places, to ascribe the limited and localized character of the San Francisco outbreak to the present immunity of the rat population.

A comparison of the natural disease in man and the experimental disease in guinea-pigs, as it existed in San Francisco, with the descriptions of the natural and experimental disease as observed in other places, will supply immediate conviction of the identity of the pathological processes. The gross lesions are characteristic and unmistakable. Moreover, the main features of the natural disease in man and the rat are easily and constantly reproducible by experimental inocula-

[1] Kitasato, Bericht über die Pest-epidemie in Kobe und Osaka, Tokio, 1900.
[2] Report of the Outbreak of Plague at Sydney, 1900.

tion. The histology of the lesions in man and animals is also in considerable accord. The primary buboes are practically identical; the necroses in the liver and spleen are easily comparable, and while, however, the proliferative nodules in the spleen, liver, and lungs in guinea-pigs may not have an exact counterpart in man, perhaps closer study of the pyæmic (metastatic) lesions in man may show that, beside necrosis and suppuration, considerable cellular proliferation has taken place. The minute changes in parenchymatous, proliferative, and emigrative cells—degenerations, necroses, etc.—are indistinguishable in man and animals.

When, therefore, the pathological anatomy, bacteriology, and the results of experimental inoculations are carefully considered, it is not easy to see by what means a part of the medical profession of San Francisco was and continues to be misled as to the nature of the epidemic disease prevailing in the Chinese quarter of that city. It is, however, due to the profession of San Francisco to state that this small number was far outweighed by those physicians who were convinced that the pest existed and expressed themselves accordingly. Among these were the bacteriologists and pathologists of the city almost without exception.

In conclusion, it is a pleasure to acknowledge the many favors conferred upon the National Commission by the local medical profession of San Francisco, and the great assistance in the scientific pursuit of the work rendered by Drs. Williamson, O'Brien, and Kellogg, of the City Board of Health, and Dr. Wilson, district physician.

THE BACTERIOLOGY OF BUBONIC PLAGUE.[1]

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Since the studies of Yersin upon plague in 1894 the bacteriology of this disease has been the subject of numerous exhaustive investigations, not only by independent workers, but also by special Commissions which European governments, namely, Austria, Germany, and Russia, have sent to India. As a result, the biological properties of the bacillus pestis and its effects upon experimental animals are well known. In a remarkably short time the chief etiological factors in bubonic plague have been revealed and effective means have been provided in Haffkine's vaccine and Roux-Yersin's serum which, together with careful isolation and thorough disinfection, have rendered it possible to check the spread and even to cure this disease. There are, however, many questions in

[1] Read before the Association of American Physicians, Washington, May 1, 1901.

the epidemiology of plague which still await a satisfactory explanation. It is not the purpose of this paper to enter into the consideration of such questions, but rather to present the bacteriological studies made by the United States Commission in San Francisco, together with subsequent experiences with the plague bacillus at Ann Arbor.

Owing to the manifold clinical features presented by the plague it will be readily seen that the greatest importance attaches to the demonstration of the presence of the pest bacillus. As is well-known, the most common type of the disease is that in which there are more or less marked enlargements of the lymphatic glands. Such buboes are usually met with in the femoral or inguinal regions, less frequently in the axillæ or in the neck. A well-marked bubonic case of plague offers no difficulty in the way of diagnosis. But, on the other hand, it must be remembered that there are cases of plague, septicæmic in character, where little or no glandular enlargement can be detected. An instance of this kind was met with by the Commission where, although the patient (Case VI.) was seen during life, it was only after the bacteriological examination of the spleen, and more particularly the positive animal experiment, that it was shown to be a case of plague. The pneumonic type of the disease was not met with by the Commission.

The detection of the plague bacillus during life is possible, but at times rather difficult. In the case of a well-defined bubo it is feasible to introduce a hypodermic needle, and in this way remove a few drops of the fluid from which cover-glass preparations and cultures may be made, and in the experience of the German Plague Commission such procedure frequently revealed the presence of large numbers of plague bacilli. At San Francisco in one living case the attempt was made to detect the plague bacillus in this way. The result in that case was negative both culturally and microscopically. The failure was undoubtedly due to the fact that the needle did not actually pierce the small gland. In suppurating, discharging buboes it frequently happens that either the pus will be perfectly sterile or it will contain only streptococci and other pyogenic organisms.

In very severe forms of plague, and, of course, in the septicæmic type, plague bacilli are present in the blood. A few drops of blood taken from the finger or from the ear lobe can be used for an examination. The number of bacilli in the blood during life is necessarily small, and for that reason their detection by direct microscopical examination is very difficult. In the experience of the German Commission, frequently where the cover-glass preparations gave negative results, the cultural methods were successful. Of 124 cases thus examined, 81 gave negative results. It is evident, therefore, that a mere examination of the blood cannot be relied upon as a means of diagnosis. The case already mentioned, where an attempt was made to discover

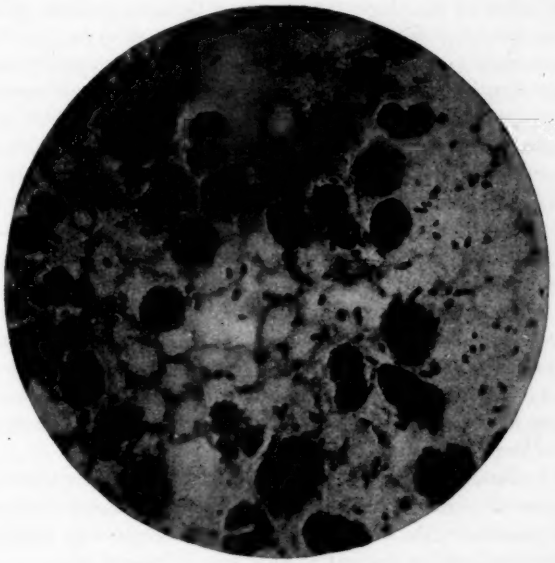
the plague bacilli in an enlarged gland two days before death, was also used for a blood examination, but with equally negative results. Only a drop of blood was used in this trial, and it is quite probable that if one or two cubic centimetres of blood had been drawn from a vein by the aid of a syringe and the amount spread over a series of agar tubes or over agar plates the result might have been otherwise.

While there is more or less uncertainty in the detection of pest bacilli *intra vitam* in the enlarged glands and in the blood of plague patients, no such difficulty is experienced in the pneumonic form of the disease. The blood-streaked sputum in such cases is, according to the experience of numerous observers, invariably rich in bacilli. A case of primary pneumonic plague which resulted from accidental laboratory infection was recently under my observation, and in this instance a microscopical examination gave an early and definite diagnosis.

In the investigation at San Francisco the Commission was fortunate enough to meet with six cases of plague. Three of these cases were seen during life, and the other three were not seen until after death. In not one of these cases did the attending physician, whether Chinese or white, call the attention of the city Board of Health to the possibility of plague being present. Indeed, this has been the history of nearly all the known plague cases in San Francisco. It was in view of the difficulty of obtaining reliable reports from the Chinese as to their sick as well as the difficulty of making satisfactory diagnoses of plague during life, or even post-mortem, that the Commission was led to formulate a recommendation which seemed to them of the very greatest importance. It was recommended that every Asiatic who had fever should be suspected as a case of infection with plague until the disease was proved to be other than plague, and every dead body should be treated as a plague cadaver until a bacteriological examination had proved the absence from the body of the bacillus pestis.

A bacteriological examination of the enlarged glands, if there are such, should be made. In several of the bodies examined at San Francisco the glands contained enormous numbers of pest bacilli, whereas in others they were less abundant. On the other hand, the spleen in five out of six cases was exceedingly rich in plague bacilli, and in only one case (Case VI.) were these present in such small numbers as to be easily overlooked in a cursory examination. Nevertheless, a guinea-pig inoculated with this spleen died in the usual time. This experience indicates the necessity of recourse to animal inoculation whenever the microscopical examination fails to give a direct and unequivocal answer. In this connection I may cite the experience of the German Commission, which, by means of the animal experiment, repeatedly demonstrated the presence of plague bacilli, although microscopically and culturally they could not be detected.

Streak preparations from the spleen or glands were usually stained with Löffler's methylene blue or with carbol-thionin. Where care is taken to avoid overheating the specimen while fixing little difficulty is experienced in obtaining the characteristic bipolar stain. Inasmuch as methylene blue is likely to overstain it should not be allowed to act for more than a few seconds. A typical preparation from a plague case will show enormous numbers of pest bacilli which are invariably single. (See Figure.) These should be examined under as high a



power as possible. A $\frac{1}{12}$ oil-immersion objective and No. 4 eye-piece will show clearly the rounded ends of the short, thick bacillus, and in addition will bring out definitely the bipolar character. As is well-known, the plague bacillus is not stained by Gram's method.

The typical short, thick bacillus is the only form met with when perfectly fresh organs of man or of animals are examined. When, however, the autopsy was delayed for some hours after death, as was not infrequently the case, a peculiar modification was to be seen. A preparation made from such material would show, beside the usual bacilli, large oval or roundish bodies which may be considered as involution forms. These peculiar modifications, as a rule, do not stain evenly, but instead show a light centre surrounded more or less completely by a deeply-stained ring or border. Because of this peculiarity they have

been spoken of not inaptly as "dough-nuts." These degenerative forms were met with in considerable number in several of the cases studied by the Commission, and were absent in but one instance (Case VI.). It may be stated incidentally that the German Commission met with these same degenerations in Bombay. As already indicated, the "dough-nut" form can be produced in animals, provided these be kept for twelve to twenty-four hours in a warm place. As is well-known, the plague bacilli are remarkably prone to develop roundish, pear-shaped, or yeast-like involution forms on dry, and especially on salt, agar.

The isolation of the plague bacillus from the fresh cadaver offers, as a rule, no special difficulty. It is very important to have a slightly alkaline medium, inasmuch as even a faint acidity exerts a marked inhibitory effect. This fact is often demonstrated in the laboratory in a most unwelcome way when such media after profuse inoculation with unquestionably viable cultures show no sign of growth. Agar plates or tubes streaked with fresh tissue invariably yield good growths, provided that the number of pest bacilli in such tissue is not too small. When only a few organisms appear to be present it is advisable to use a larger amount of material for inoculation. As a matter of fact, even when the tissues are extremely rich in pest bacilli the number of colonies which develop on agar is often considerably smaller than might be expected, showing that many of the organisms are considerably enfeebled. This condition is especially met with when tissues are derived from animals which have been dead for many hours. The involution forms which are present in such cases are apparently incapable of development on artificial media.

The inoculation of such material, however, into a susceptible animal will cause death, and from the fresh organs thus obtained cultures can be readily secured. As will be indicated presently, the guinea-pig can hardly be considered as among the most susceptible animals.

The cultural characteristics are well-known, and need not be elaborated upon in this connection. They are, moreover, described, though briefly, in the appendix.

For the purpose of diagnosis the direct microscopical examination is, as a rule, sufficient. When, however, the pest bacilli are very few, or when other organisms are present which tend to mislead in the identification, it is then necessary to resort to animal inoculation in order to arrive at a satisfactory conclusion. A portion of the gland or spleen should then be introduced under the skin of an animal. The common rat, in the experience of others, is by far the most susceptible animal, and should be used whenever possible. Inasmuch as rats were with difficulty obtainable at San Francisco, the experimental inoculations were confined to guinea-pigs, which usually died in from three to five days after such inoculation. Exceptionally, a guinea-pig may die in

thirty-six hours or even less, and I have repeatedly observed death to be delayed for ten or twelve days. This is especially true when pure cultures rather than bits of tissue are introduced into the animal. It may, indeed, happen that pure cultures, recently isolated from man or animals, will fail to kill guinea-pigs.

The failure at times of pure cultures of pest bacilli to kill guinea-pigs indicates in the first place the labile character of the virulence of these organisms when grown on media which have an even slightly unfavorable composition or reaction. Moreover, it shows that the guinea-pig offers considerable resistance to infection, and that the survival of such an experimental animal does not positively exclude the presence of plague bacilli. The virulence of these organisms can often be restored by frequent transplantation to fresh distinctly alkaline media, and especially by the use of the collodium sac method.

The effects observed in guinea-pigs varied somewhat with the duration of the disease. Where death occurred in less than two days little or no structural change was observable. Usually, as a result of subcutaneous infection, the inguinal or axillary glands were considerably enlarged. Inasmuch as the changes which take place in the glands, spleen, and other organs will be treated by Dr. Flexner, it will be unnecessary to describe these in this connection. I may add, however, that exceptionally well-marked pneumonia occasionally, though rarely, may be observed in guinea-pigs following subcutaneous injection. In one instance recently observed the pneumonic process was associated with pericarditis, the pus of which yielded a pure culture of plague bacilli.

The direct detection of the plague bacilli in the tissues of the six cases studied in San Francisco, the cultural properties of the organisms isolated from these cases and the successful animal inoculations demonstrated the existence of the plague in that city. If any additional proof as to the nature of these organisms and of the disease existing there were necessary it has been recently furnished by the accidental development of a case of acute pneumonic plague in one of the workers in the Hygienic Laboratory of the University of Michigan. The young man referred to had been engaged for some months in the preparation of Haffkine's vaccine and Lustig's serum.

A highly virulent California culture was employed in this work. In some unknown way, possibly through the use of a pipette or soiled finger, the organism was introduced into the mouth, and a very acute infection followed. The young man was taken sick on Wednesday evening, April 4th, and complained of intense backache. The temperature rose in a few hours to 102° and more. Toward morning he vomited twice a greenish, bile-stained fluid. At noon that day I learned for the first time of his illness, and with Dr. Vaughan visited him in

the afternoon. When seen his temperature was 102.8°; his eyes were bloodshot, and he complained of severe headache; the pulse was rapid, and the pulmonary distress was marked. It was clearly a very severe acute infection, and, knowing the kind of work he was engaged in, it was decided to give him at once an injection of Yersin's anti-pest serum. Twenty c.c. of this serum were given at 4 o'clock that afternoon. At the same time the tonsils and the inside of his mouth were rubbed with swabs, and the material thus obtained was planted on agar, and cover-glass preparations were also made. These showed a large number of ordinary mouth germs, but nothing that could be identified as plague bacilli. The cultures, it may be added, when developed were likewise negative, and when injected into a guinea-pig had no effect. At 8 o'clock in the evening the patient coughed up for the first time a small bit of blood-stained sputum. This was examined at once, and on staining showed plague bacilli. Accordingly the patient was removed immediately to the isolation hospital, and his room was locked up and thoroughly disinfected with formaldehyde.

After arrival at the isolation hospital, with the knowledge that we had to deal with a case of acute primary pneumonic plague known to be almost invariably fatal, intravenous injections were decided upon as offering the only possible chance for recovery. Accordingly 20 c.c were injected intravenously at about 11 o'clock that night. The next morning, the temperature still persisting at about 104°, a second intravenous injection of like amount was given. Even this showed no marked effect, and as the temperature reached 105.3° at one time, and the patient was becoming markedly apathetic, a third injection was made. This time 20 c.c. were injected intravenously and 40 c.c. subcutaneously. All told, he received within twenty-four hours after he was seen by us 120 c.c. of serum, one-half of which was injected intravenously. Within a few hours after the last injection the temperature dropped to 100°, and before the end of the third day of his illness it reached the normal. With the exception of an attack of heart failure caused by his attempt to sit up on the fourth day, and the serum effects, such as swollen joints and hives, which developed a week later, the patient made a complete recovery. Extreme cardiac weakness was a noticeable symptom, which persisted for more than two months after the onset of the disease.

It should be added that the animal experiment eventually confirmed the original microscopical diagnosis. A guinea-pig inoculated with the sputum raised at the end of the first day (Thursday evening) died in four days of typical plague. It is further noteworthy that a second guinea-pig inoculated with sputum rich in plague bacilli which was raised Saturday morning after the temperature had fallen remained alive.

Appendix.

Under this heading I have placed the description of the bacteriological work done on the six cases of plague which were studied in San Francisco by the commission. It should be stated that this matter forms part of the report of the commission as published in the *Public Health Reports* of the United States Marine Hospital Service.

Case I.—Chun Ah Chou, 814 Washington Street; necropsy February 5th. The spleen and left femoral glands were examined. These organs were found to contain enormous numbers of bacilli having the morphological and tinctorial properties of bacillus pestis; thus the short, thick, oval rods gave a bipolar stain of the Löffler's methylene blue or with carbolic thionin and were decolorized by Gram's method. Their pathogenicity was determined by inoculation of portions of the spleen and of a pure culture, subcutaneously, into guinea-pigs.

Agar streaks made from the perfectly fresh organs showed many small white, moist isolated colonies, having all the appearance of those of bacillus pestis. This was further confirmed by microscopical examination of living and stained preparations of such cultures. A few rapid growing colonies due to other forms of bacteria were present. Subcultures were made in glucose gelatin, bouillon, agar, salt agar, and milk. On agar in Petri dishes in twenty-four to forty-eight hours in the incubator, small white or grayish, moist colonies developed. These had finely granular centres, with a smooth, sharply defined border.

The stab-culture in glucose gelatin developed a slight growth along the line of inoculation. On the surface the growth spread slightly, was grayish, moist in appearance, and had a slightly wavy, raised border. No gas was formed.

In bouillon, in twenty-four hours, a diffuse cloudiness was produced. The sediment was very slight, scarcely appreciable. Subsequently, a faint stringy deposit formed. The surface remained perfectly clear with a trace of a ring or collarette.

The streak cultures on nutrient agar presented a moderate grayish-white, moist growth which, when touched with a platinum wire, could be drawn out into strings.

On 5 per cent. salt agar the growth is very slight, scarcely visible, and shows the peculiar roundish or pyriform involution forms of the pest bacillus.

In milk the organism grows without producing any visible change in the medium.

The absence of gas production and of coagulation of milk, together with the macroscopical and microscopical characteristics, agreed fully with the properties of bacillus pestis. The effects on animals have been described in a preceding part of the report.

Guinea-pig No. 1.—Was inoculated under the skin with a portion of the spleen from the above case. It died in thirty-six to forty hours. Cultures on agar made from the spleen and heart's blood gave almost pure growths of the pest bacillus. Direct examination of the organs showed enormous numbers of typical plague bacilli.

Guinea-pig No. 2.—Was inoculated subcutaneously with a pure culture obtained from the gland of above case. The animal died in three

days. Plague bacilli were very numerous in the spleen and inguinal glands, and were also present in the heart's blood.

CASE II.—Lum Hong Yuen, 28 Ross Alley; necropsy February 6th. Smear preparations from the spleen showed large numbers of short, thick rods, chiefly single; some oval or roundish forms were also present. The organisms stained readily with Löffler's methylene blue or with carbolic thionin. In the latter case the bipolar staining was excellent. The organisms were completely decolorized by Gram. Cover-glass preparations from the gland likewise showed very numerous bacilli, occurring singly, taking the bipolar stain, but not that of Gram. Agar cultures were made at the time of the necropsy in the undertaker's shop of Main Fook. The cultural and morphological characteristics were the same as those observed in Case I.

Guinea-pig No. 3.—Received subcutaneously a portion of the spleen from above case; died in five and one-half days. On autopsy the spleen was found markedly enlarged, full of white nodules which were also present in the liver and in the lungs. Cover-glass preparations from the spleen showed enormous numbers of bacilli, having all the characteristics of bacillus pestis. Agar slants were inoculated with the heart's blood and spleen of this animal. The former yielded a slightly contaminated growth, but the culture from the latter was pure.

CASE III.—Wong Chi Lui, 21½ Waverly Place; autopsy February 7th. Streaked preparations from the spleen showed very numerous pest bacilli apparently in pure culture; the predominating form was the short, thick rod, although some oval or roundish forms were present. Löffler's methylene blue and carbolic thionin stained the bacilli readily, demonstrating the characteristic bipolar form. The organisms were completely decolorized by Gram. Similar preparations made from one of the left femoral glands showed fewer organisms, but these in form, size, and staining reactions are identical with those found in the spleen. Cultures made on agar developed very slowly; on subsequent transplantation, however, the growth was more rapid, more abundant, and typical of that of bacillus pestis.

Guinea-pig No. 4.—Was inoculated subcutaneously with a portion of the gland from the above case. Death resulted in three and one-half days. Bacilli were numerous in the spleen and corresponded in characteristics to those of the plague bacilli.

Guinea-pig No. 5.—Was inoculated subcutaneously with a portion of the spleen; it was found dead three and one-half days later. Numerous plague bacilli were found in the spleen, heart's blood, and glands. Agar streaks from the heart's blood gave numerous small colonies of pest bacilli with a few larger colonies due to foreign organisms. The spleen gave numerous isolated small moist colonies, apparently a perfectly pure culture of the plague bacillus. Agar streak plates were made at the same time, and gave in twenty-four hours numerous minute colonies.

Guinea-pig No. 6.—A portion of the spleen from this case was introduced into the peritoneal cavity. Death resulted in four and one-half days. Pest bacilli were abundant in the internal organs and in the glands. Agar streaks from the heart's blood gave a very limited growth, while that from the spleen was scarcely visible. In this and several other instances difficulty was experienced in starting the growth

of the organism directly from the tissues. Once started, however, with subsequent transplantations, better results were obtained.

Guinea-pig No. 7.—Was inoculated subcutaneously with a loopful of a pure culture obtained from Guinea-pig No. 5. It died in two and one-half days. Necropsy revealed a hemorrhagic œdema, and cover-glass preparations of this showed pest bacilli mixed with numerous minute diplococci and streptococci. The spleen was large and soft, contained nodules, and on staining cover-slips therefrom enormous numbers of typical plague bacilli, apparently perfectly pure, were found. No diplococci were present.

Case IV.—Tom Shom, 814 Washington Street; necropsy, February 11th. During life some fluid was aspirated by means of a sterile syringe from the swelling in the right femoral region and transferred to nutrient agar. Blood was also drawn from the lobe of the ear and planted on agar. Stained preparations made from these specimens failed to demonstrate the presence of any organism. Cultures developed pyogenic cocci, but failed to give any indication of pest bacilli. On necropsy, the femoral glands, though characteristic of plague, were found not markedly enlarged. It was evident that the aspirating needle, when introduced, had missed the gland proper, and the failure to isolate the pest bacillus during life in this case can thus be explained. It should be noted that the periglandular tissue was but very slightly involved. Streaked preparations made from the hemorrhagic gland showed relatively few typical plague bacilli. A long, thick bacillus was present in small numbers. Gram's stain was negative. Streaked preparations from the spleen showed the pest bacillus to be present in large numbers and apparently pure. The organisms occurred singly, gave the bipolar stain, and were decolorized by Gram.

Guinea-pig No. 8.—Was inoculated subcutaneously with a portion of the spleen from this case. Six and a half days later, though healthy in appearance, it was killed. A circumscribed caseous local lesion was found. There was a slight glandular enlargement on the same side. The spleen was slightly enlarged and showed white nodules. Pest bacilli having the short rod and oval form were present in small numbers.

Case V.—Ung Ah Buck, St. Louis Alley; necropsy, February 12th. Cover-slip preparations from the cervical glands showed the presence of several distinct organisms. The short, thick, oval forms of the pest bacillus were present in small numbers. With them was associated a large thick bacillus; there were also bacilli present resembling the bacillus diphtheriæ and a diplococcus closely resembling that of Fraenkel. The pest bacilli gave the usual bipolar stain with methylene blue and with carbolic thionin. Specimens stained by Gram's method showed deeply stained diplococci, the other forms being decolorized. Smear preparations from the spleen showed many organisms resembling the bacillus pestis morphologically.

Agar streaks from the fresh spleen gave a number of discrete moist colonies which consisted of large, oval, non-motile bacilli, occurring singly and only occasionally in pairs; the streak cultures from the cervical gland also gave numerous isolated colonies. In both cases the cultures obtained were apparently perfectly pure and agreed in every respect with those of plague bacilli. The other bacteria seen in cover-slips did not grow. Agar plates yielded the same results.

Guinea-pig No. 11.—Was inoculated subcutaneously with a small portion of the spleen from above case. In about three days the animal was very sick and was finally killed five and one-half days after inoculation. Bacillus pestis was found in the spleen and to a less extent in the blood.

Case VI.—Foong Ah Fong, 747 Sacramento Street; necropsy, February 12th. Streaked preparations from the spleen revealed the presence of pest bacilli, although these were not very abundant; indeed, they were difficult to find in cover-slips. Typical bipolar staining rods and oval, roundish forms were, however, found. Gram's stain was negative.

Streak cultures were made with the fresh spleen on agar slants, and at the same time agar plates were made. The agar streaks failed to give an appreciable growth, but on the plate a colony was found which corresponded to that of the plague bacillus. On microscopical examination it was observed to consist of small, short, oval, non-motile rods, which decolorized by Gram. The colony transplanted to agar gave a typical growth of pest bacilli, and this culture was used to inoculate guinea-pig No. 10.

Guinea-pig No. 9.—Received a portion of the spleen of Foong Ah Fong subcutaneously. It died in four and one-half days. The spleen contained enormous numbers of pest bacilli, which stained in the usual bipolar manner and were decolorized by Gram. The heart's blood likewise contained the organism. Cultures were made on agar from the spleen and heart's blood of this animal; both gave numerous small, moist colonies of bacillus pestis.

Guinea-pig No. 10.—Was inoculated subcutaneously with the agar culture mentioned above. It was killed two and one-half days later. The spleen showed only a few but characteristic pest bacilli. Under the skin there was but slight local change and a few typical bacilli were found.

The bacteriological examination of the foregoing six cases has, therefore, demonstrated the presence of the bacillus pestis in each.

A CASE OF MALARIAL NEPHRITIS, WITH MASSING OF PARASITES IN THE KIDNEY.[1]

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The frequent occurrence of renal lesions in malarial fever was described long before the discovery of the malarial parasite, and has been very constantly recognized throughout the progress of our knowledge of the disease.

Owing to the studies of Rempicci in Italy and of Thayer in America it is unnecessary to again review in detail the contributions of the

[1] Read before the Association of American Physicians, Washington, May 2, 1901.

various observers in this important field. On the evidence collected and largely contributed by these two writers one may now state with confidence that albuminuria is nearly constantly present in pernicious æstivo-autumnal infections and is frequently observed in the milder tertian cases. Of greater interest and importance are the rather numerous records of distinct signs of an acute exudative process in the kidneys, usually in æstivo-autumnal cases, less often in tertian infections, and consisting in the presence in the urine of epithelial and granular casts, many blood cells, as well as considerable albumin. Although the milder changes in the urine may develop, according to Rempicci, either during or shortly after the acute attack, it would seem that the more severe urinary signs can be safely attributed to the malarial infection only when arising in the course of a pronounced acute seizure.

Recovery has usually followed the acute symptoms, but Kelsch and Kiener, Laveran, Marchiafava and Bignami, Rempicci, and Thayer have described various types of chronic nephritis occurring in long-established or chronic cases of malaria, while Kelsch and Kiener state that the chronic nephritis of malaria is distinguished from other types by the prominence of hemorrhages and the comparative absence of fatty and hyaline degeneration and of arterial changes.

The acute nephritis of malaria is almost never immediately fatal, so that the pathologist must speak with reserve regarding the origin and significance of many of the cases of exudative nephritis commonly attributed to malaria. In view of the frequent clinical reports of the presence of considerable albumin, many casts, and of blood cells in the urine, and less often of œdema and mild uræmic signs in the disease, it seems certain that during severe malarial infection a true exudative nephritis is sometimes excited. Even in the absence of pathological examination of the kidneys these symptoms may with some confidence be referred to congestion of vessels, acute degeneration of cells, and exudation of serum and diapedesis of red cells from the bloodvessels, all dependent upon the action of the malarial toxin upon the renal tissue.

Coming, now, to the fatal cases of pernicious malaria in which there has been a microscopical examination of the kidney, the conditions found in this organ in all except hæmoglobinuric cases have been very uniform. The lesions observed have been those of a severe acute degeneration of the cortical tubule cells, with moderate exudation of albumin into the tubules and glomeruli.

The chief contributions in this field have come from Guarnieri, Marchiafava and Bignami, Monti, Bastianelli, Barker, and Benevenuti. In all of the reports of these observers the nephritis has been clearly of toxic origin, while the number of parasites found in the kidney has been small, although they were usually very numerous in other tissues. The

single exception to this rule is found in one of Barker's cases, in which death and probably the recent changes in the kidneys were principally referable to general infection by streptococcus pyogenes Here the renal capillaries were frequently thrombosed by masses of streptococci and large numbers of tertian parasites. This case cannot, therefore, be regarded as one of malarial nephritis, but rather as an example of pyæmia or septicæmia terminating the usual benign course of a tertian malarial infection.

The invariable freedom of the kidney from localization of parasites in pernicious cases cannot be attributed to the phagocytic powers of this organ, which enjoys only a moderate capacity to destroy parasites. Guarnieri, who noted the small number of parasites in the kidneys of his and other cases, referred this comparative immunity to the rapid circulation of the organ.

The examination of the records of microscopical examinations of the kidneys in malarial fever fully warrants the latest conclusions of Marchiafava and Bignami regarding the origin of the renal changes in pernicious malaria, which are as follows, quoting from their article in the *Twentieth Century Practice:*

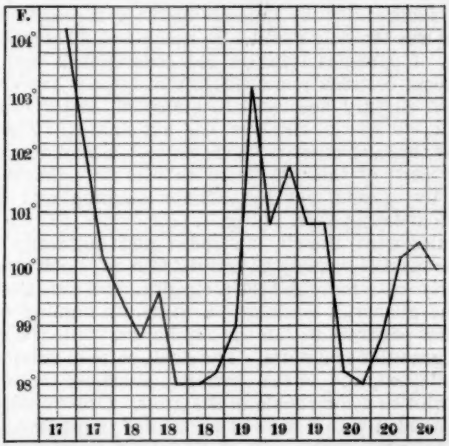
"As to the pathogenesis of the renal lesions in malarial infections, we are at present able only to form theories. The knowledge of the parasite has so far thrown no light on the pathogenesis of the nephritis. In pernicious infections very few parasites are found in the kidneys even when the changes in the epithelium may be so grave as to lead to necrosis. From this fact we may infer that the lesions are due not to a localization of parasites in the renal capillaries, but to some toxic substance eliminated by the kidneys."

My own experience in the examination of fourteen fatal cases of malaria, seen mostly at Montauk in 1898, fully accorded with the above conclusion, as I found, usually, extensive degenerative changes in the kidney, once the lesions of hæmoglobinuric malaria, but comparatively few or no parasites in the renal vessels. The present case, recently encountered, developing in the vicinity of New York, showing the clinical symptoms of acute hemorrhagic nephritis, with partial suppression of urine, and giving clear microscopical evidence of extreme massing of parasites in the kidney, with various mechanical lesions resulting from their presence, seems to require a reversal of the above conclusion, and appears to show that malarial nephritis may be caused principally or in large part by the presence of an excessive number of parasites in the renal capillaries.

Clinical History. The patient was a friendless girl, aged seventeen years, a Slav, who had been in America one year. She had enjoyed good health until going as a servant to College Point, Long Island, in July, 1900. She was discharged early in September on account of an

alleged "inability to work," and this fact, together with a distinct pallor and slight jaundice, noted on her return to the city, indicate that she had suffered for some weeks from malaria contracted on Long Island. On September 12th she was taken acutely ill, with chills and fever, and, being without the help of a physician, she became steadily worse until brought by an ambulance to the hospital, on September 17th.

On admission the patient was well nourished; tongue moist, slightly coated, prostration marked. Physical examination of lungs, heart, and liver was negative. The area of splenic dulness was enlarged, but the organ was not palpable. There was slight œdema of the legs. The urine, voided naturally in moderate quantity, was described as of high color, clear, acid in reaction; specific gravity, 1018; urea, two and one-half grains to the ounce; albumin, 2 per cent. by volume; sugar absent. Microscopically there were noted: epithelial cells, many red blood cells, and amorphous urates; diazo reaction marked. Temperature, 104.2°; pulse, 98. On September 18th there was vomiting of



food and medicines; constipation relieved by enemas; and retention of urine with marked diminution in its quantity, which continued until death. Delirium developed on September 19th, and was controlled by morphine, sulphonal, and choralamid, given at intervals, on the 19th and 20th. On the 19th she vomited a round worm and was given at intervals three doses of santonin, three, five, and fifteen grains, without any change being noted in the urine, stools, or conjunctiva. Delirium continued on the 20th, and, the pulse failing steadily, she became comatose and died at 9 P.M. The four-hourly temperature-chart is appended. The clinical diagnosis was typhoid fever, with acute nephritis.

Autopsy, by Dr. Otto Schultze, thirteen hours after death. Body well nourished; rigor well marked. *Heart* normal. An ounce of straw-colored fluid in pericardium. A few ecchymoses in visceral pericardium. *Lungs:* Few old pleural adhesions. A few ecchymoses in visceral pleura. *Liver* appeared normal. *Pancreas* normal. *Stomach* normal. *Ileum* congested, solitary follicles moderately swollen. *Colon*

congested. *Spleen* much enlarged. Weight, sixteen ounces; consistence firm; Malpighian bodies prominent; pulp dark red. *Kidneys* together weighed sixteen ounces; consistence reduced; capsule free; cortex remarkably light in color; medulla and papillæ extremely dark, and slightly rust-colored; cortical markings entirely obscured. In the cortex of the right kidney there is a superficial anæmic infarct with surrounding hemorrhagic zone. This infarct measures $3\frac{1}{2} \times 2$ cm. in area, and 2 mm. in depth.

Anatomical Diagnosis. Acute hemorrhagic nephritis. There was still no suspicion of malarial infection. Cultures of liver, spleen, and kidney yielded bacillus coli and putrefactive species.

Through a misunderstanding, all the viscera, except the kidneys, were thrown away. The kidneys were hardened in 5 per cent. formalin and examined microscopically.

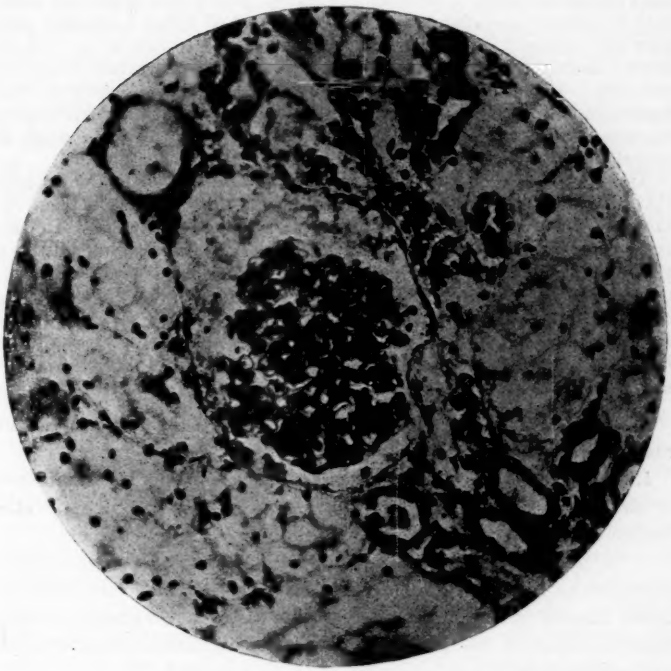
Microscopical Examination of Kidneys. After the malarial infection was suspected, on account of the peculiar pigmentation of the glomeruli and straight vessels, thin sections cut in celloidin and paraffin were stained most successfully by Nocht's method, as employed for blood smears. This was the only method by which I could secure a blue color in the bodies of parasites lying in red cells stained deeply by eosin. For this purpose sections remained in the dye for twenty-four hours, and were then slightly decolorized in alcohol, and cleared in oil of cajuput. The chromatin, however, was not stained. The changes demonstrated by this and other methods were of a most remarkable type.

The lining cells of the convoluted tubules were almost entirely destroyed, not by erosion, but by extreme swelling and degeneration, apparently of hydropic type. (Fig. 1.)

These tubules were thereby distended and uniformly filled by an indiscriminate mass of vacuolated cell detritus in which pyknotic nuclei were irregularly scattered. All the cortical tubules were about uniformly affected. The glomeruli contained a moderate number of pigmented cells and a few parasites within the capillaries, while the capsules were distended by granular coagulum. The small cortical vessels were almost invariably collapsed, and to this perfectly bloodless condition must be ascribed the whitish color visible in the gross. Occasionally a capillary was found distended with a mass of pigmented parasites.

In the medulla the lining cells of all tubules were markedly eroded. In this region most of the capillaries were filled, and many were distended with masses of infected red cells and pigmented parasites which had nearly destroyed the red cells. (Fig. 2.) Many of the distended capillaries were ruptured, and the tissue was studded with miliary hemorrhages, about some of which a few leucocytes, mostly mononuclear, were gathered. The parasites were of small and very uniform size, but richly pigmented. They were identical in appearance with the full-grown forms of the æstivo-autumnal parasites seen in sections of tissue of other cases in which these parasites were identified in the blood during life. Very few rings or rosettes could be discovered, so that the brood was unusually compact. (Fig. 3.) Their numbers and compact massing were similar to what I have seen in other fatal cases in which the parasites were massed in the brain, heart muscle, or bone-marrow. The discharging tubules were distended with casts, usually coarsely granular, sometimes entangling infected red cells and pigmented leucocytes. Some infected red cells lay free in the lowest discharging tubules.

FIG. 1.

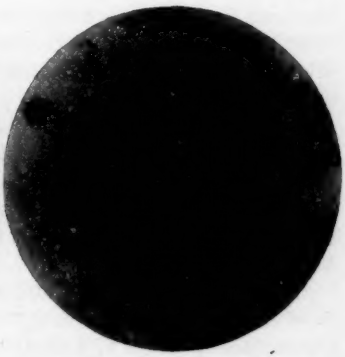


Convoluted tubules and Malpighian body. × 250.

FIG. 2.

Malarial parasites in kidney. × 250.

FIG. 3.



Parasites in renal capillary. × 1000.

The infarcted area in the right kidney was in an early stage of coagulation necrosis. All the capillaries about this area and many within it were distended with blood cells, most of which contained parasites and pigment. Many of the vessels leading to this area were distended to two or three times their natural calibre by thrombi of infected red cells. The infarction is clearly referable to the plugging of small vessels, mostly capillaries, by thrombi of infected red cells. The number of parasites in this cortical zone and throughout this section of the medulla was greater than I have ever seen in any other tissue.

The following *summary* presents the lesions observed in the kidneys: Extreme and peculiar degeneration of lining cells of all cortical tubules. Distention of capsules of glomeruli by granular albuminous coagulum. Occlusion of most cortical capillaries by the distended tubules. Large superficial red and white infarction, from occlusion of vessels by thrombi of infected red cells. Numerous miliary hemorrhages, from rupture of distended capillaries. Distention of nearly all capillaries in medulla and papillæ by infected red cells and parasites. Casts in discharging tubules, consisting usually of coarsely granular material, but sometimes entangling infected red cells and pigmented leucocytes.

EPICRITICAL. The following questions arise concerning the significance of the above findings:

1. Is it possible to draw any conclusions regarding the significance of the renal lesions on account of the failure to examine the other viscera microscopically?

2. Is the present case a true example of massing of æstivo-autumnal parasites in the kidney comparable to the cases in which they have been found massed in the brain in comatose cases, in the gastro-intestinal tract in choleraic cases, in the heart muscle in cardiac cases, or in the marrow as observed in a case of pernicious anæmia?

3. What is the origin of the extreme degeneration of the cortical tubules?

1. To the first question there can be no hesitation in answering that the renal lesions are in themselves sufficiently distinct to stand as the chief feature of the case. Doubtless there were many parasites in the other viscera, but where pigmented parasites are extensively massed in any tissue gross evidence of their presence may be detected in the excessive pigmentation and extreme blood content of that tissue. No such evidence being present in the gross appearance of any other viscus, it is safe to conclude not only that the kidney contained an excessive proportion of parasites, but that they were not excessively numerous in any other locality. The clinical features of the case also support this belief.

2. It is equally clear that the case is one of true malarial nephritis in which a peculiar hemorrhagic character of the lesion is referable to the mechanical effects of massing of parasites in the renal tissue. This lesion is not to be classed with the usual type of renal lesion in malaria, which is an acute degeneration referable to the general toxæmia of the

disease, and in which comparatively few parasites have heretofore been found in the kidney. Enormous numbers of parasites in the capillaries, thrombosis of many vessels, and multiple hemorrhages are the specific lesions observed when the parasites have been massed in the brain, gastro-intestinal tract, heart muscle, and marrow.

3. The extreme degeneration of the cortical tubules seems also to be a somewhat peculiar feature of the present case. In the reported cases of malarial nephritis of purely toxic origin the degeneration of tubule cells has often been extreme, but it has always been of a different type from that described above. In fourteen cases which I have examined the degenerative changes have always been much less advanced and of a different type from those of the present case. Although much of the change in the tubule cells was doubtless owing to the general toxæmia of the disease, I am inclined to refer the peculiar character of the process and its extreme degree to the presence of so many parasites in the tissues acting principally through obstruction of the circulation.

Finally, it is important to consider the possibilities of diagnosis during life of this type of malarial nephritis. From the clinical examination of the urine and the microscopical appearance of the discharging tubules in the kidney it seems probable that a diagnosis of this type of malarial nephritis may be established during life on the following evidence, to be obtained from the urine. Partial or complete suppression of urine; considerable admixture of intact red cells; a considerable proportion of albumin; the presence of many coarsely granular, epithelial, and some blood casts; the presence of *infected red cells*, both free and adherent to casts, and of pigmented leucocytes adherent to casts.

The present case, while demonstrating the existence of a specific type of malarial nephritis, yields no new indication why the æstivo-autumnal parasite selects certain viscera for its chief attack, and demonstrates no new character in the pathogenic action of this protozoon.

There is no known reason why the bronchopulmonary mucosa, or that of the colon, or the serous membranes, or the skeletal muscles, should not suffer in the same way as do the brain, the gastro-intestinal mucosa, the heart muscle, and the marrow. The kidney may be specially exempt on account of its rapid circulation, as suggested by Guarnieri, but apparently it does not always escape. The actively phagocytic viscera, the liver, and spleen, seem capable of rapidly destroying the enormous influx of parasites which frequently reaches their capillary systems. Yet the lymphoid marrow, with its more complex circulation, is known to be less resistant than the spleen and lymph nodes.

These two factors, however—rapid arterial circulation and active phagocytic powers—seem to be the only qualities which can preserve a tissue from occasional overwhelming growth of the æstivo-autumnal parasite.

Microscopical examination of the kidneys of fatal cases of malaria has, then, yielded evidence of three main types of acute renal lesions occurring in this disease.

1. Acute degeneration of toxic origin, often reaching a degree in which exudation of blood serum into the tubules is added. This lesion is responsible for the vast majority of the cases of albuminuria in malaria.

2. An extreme form of acute degeneration, with focal necroses, numerous hemorrhages, and exudation into the tubules of blood serum and blood pigments. This lesion is seen in cases of hæmoglobinuric malarial fever, and it has not yet been found associated with an excessive number of parasites in the capillary vessels.

3. Massing of parasites in the renal capillaries, with extreme degeneration of parenchyma cells, multiple hemorrhages, and exudation of blood serum into the tubules. It seems certain that this type of lesion can occur only in severe æstivo-autumnal infections.

There is anatomical evidence that in the pernicious æstivo-autumnal cases the three types of lesions may be variously combined, but no good reason for believing that with the benign tertian infection occurring in this latitude any other than the first type can exist.

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INFLUENZA AS A CAUSAL FACTOR IN ACUTE MASTOIDITIS AND THE EARLY TREATMENT.[1]

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The importance of the relation of influenza or la grippe to acute mastoiditis has been fully demonstrated, to my satisfaction at least, by the number of cases coming under observation within the past few years. Reviewing the literature of acute mastoiditis, one is impressed with the fact that the large majority of cases are associated with or

[1] Read before the Eastern Section of the Laryngological, Rhinological, and Otological Society, at Buffalo, N. Y., June 21 and 22, 1901.

immediately follow epidemics of influenza. To be clearly understood, I will state in the beginning that it is accepted that mastoid complication following influenza is consequent upon tympanic infection; therefore, in all of these cases we have to deal with a tympano-mastoiditis. I am convinced that the mastoid antrum at least is involved in most, if not all, grippal infections of the middle ear; the further extension would seem to depend upon the character and virulence of the infection, and possibly upon its association with other infection, the age of the patient, and our proper estimate of the early treatment. Influenza is defined as an infectious disease due to Pfeiffer's bacillus, and characterized by inflammatory symptoms of the respiratory tract, digestive and nervous systems, accompanied by prostration and a marked tendency to complications. The conditions found in the upper respiratory tract concern us most, on account of the direct bearing upon our subject. The phenomena found here are irregular; in some the mucous membrane is thickened, irritated, and swollen; pain and discomfort complained of, out of all proportion to the appearances; in other cases we find a more intense congestion of the mucous membrane, less swelling, and a tendency to the formation of small blood clots here and there over the surface. I speak of these to call attention to the fact that the writer in his experience has found practically the same peculiar differences in middle-ear complications following grippal infection, and which we think have a direct bearing upon the character of the mastoid involvement. It has been my good fortune to see, in the last three epidemics of influenza, a large number of cases of complicating otitis media and mastoiditis, and I have been forced to the conclusion that there is a great difference in these two varieties of infection. The former is apt to come on during convalescence or following the attack; the patient complains of an uncomfortable feeling in the ear, gradually changing to severe pain in from twelve to twenty-four hours. Examination usually reveals the membrana tympani moderately congested, no decided bulging, and, to all appearances, a mild case of otitis media. From this time on the character of the case changes; there is developed mastoid tenderness on deep pressure, or the slightest suspicion over the tip, or it may be absent entirely. Bulging of the membrana flaccida becomes very pronounced, and the pain excruciating. There is in these cases an almost simultaneous invasion of the tympanum, antrum, and cells with the infectious and suppurative process, and their integrity is rapidly encroached upon. After incision of the membrana tympani, regardless of the thoroughness with which it is done, there is a continued copious purulent discharge. The amount and rapidity of pus formation is astounding. The incision fails to take on a reparative process, the lips remain open, pouting, and, in some, necrotic, the whole picture giving one the impression of a very active suppurative process in tissue

of low vitality. *I have seen very few of this type of cases escape an active and rapid involvement of the mastoid.* The latter variety we find coming on more often during the attack; the patient complains of sudden severe pain in one ear, followed, it may be in two or three days, by the same in the other. There may be a slight blood-tinged serous discharge and some mastoid tenderness. Examination in these cases gives us an entirely different picture; the membrana tympani is intensely congested, with small hemorrhagic areas over its surface, which appear to be between the layers of the membrane, giving it the appearance of marked bulging. I have seen this hemorrhagic condition extending well along the cutaneous covering of the bony canal. These cases, while to all appearances they would indicate a much more severe condition, in the writer's experience have yielded more readily to conservative measures of treatment. Influenza, as a causal factor in tympano-mastoiditis, is being recognized, and its importance given much consideration by some of our best observers. Kyle, in a paper read before the Southern Section of this Society last December, is very explicit on this point. He says: "This infection has a curious way of affecting and penetrating certain tissues, cavities, and locations of the mucous membranes which is peculiar to itself. I have seen following the attack of la grippe, or associated with it in most rapid succession, an involvement of the middle ear, this involvement being of an infectious nature and rapidly going on to suppuration. I have seen both middle ears involved, with associated involvement of both mastoids, the involvement being rapid and virulently infectious." Knapp says: "The grippe is a frequent cause of mastoid caries," and reports a number of cases in support of his views.

A point of great importance to be kept in mind in dealing with this particular infection is the great rapidity of its progress and its usually virulent nature. The writer called attention to this fact in a paper read before the Jefferson County Medical Society, July, 1900, and published in the *Laryngoscope*, February, 1901. I can do no better than quote my words at that time: "There is great necessity of a thorough examination in all cases of suppurative middle-ear disease with a view of determining the extent of the process, and especially so in cases complicating influenza, as I have come to look upon this particular infection with greater anxiety regarding the dangerous complications than any other we have to deal with. When once beyond the tympanic cavity its virulence is shown by rapid destruction of the mastoid walls, and if not relieved by surgical interference it is apt to involve the meninges and brain in a purulent inflammation."

In my humble opinion I believe la grippe infection is responsible for more cases of acute suppurative mastoiditis than either scarlatina, measles, or diphtheria. My clinical experience bears me out fully in

this statement. The results of Perez, in his recent experiments with Pfeiffer's bacillus to determine the influence of virulent cultures upon traumatism, do not agree with clinical experience. He made a number of inoculations—150 injections in all—into the different cavities and organs of the body, and in all obtained equally unsatisfactory results. The peritoneal and pleural cavities, brain, eye, ear, and joints were all successively injected. But five cases of purulent otitis occurred after twenty injections of the middle ear. From his results the author expresses the belief that Pfeiffer's bacillus does not cause infection, but an intoxication, and its pathogenicity is due to a toxin. This may explain the difference in the different varieties of tympano-mastoiditis referred to above; it may be that in one we have an inflammation due to the inoculation of the Pfeiffer bacillus alone, whereas in the other variety it may be associated with a pyogenic organism, and the virulence of each thereby increased. The rapidity of the invasion and destructive process would indicate some such combination of influence. Although a great deal has been said and written in the past few years on the early or abortive treatment of acute mastoiditis, it would seem to me that from the number of different views and different methods employed there is still ground for discussion. I have used the Leiter ice-coil or ice-bag advised by McKernon; heat externally and hot douching, advocated by Roosa; leeching, as recommended by Bacon, with rest, cathartics, etc., and found each has its advantages in certain selected cases. I would strongly emphasize the fact that in the early treatment of these cases we should not expect to take any one method and apply it indiscriminately to every case of acute tympano-mastoiditis that comes under our observation any more than we would take one method and apply it in any other class of cases. Great care should be exercised in selecting our cases for this or that method of treatment, for much depends upon good judgment in the early stage. This fact alone, I think, will explain in a measure the great discrepancy in the results obtained by different observers when using the same line of treatment. If we see these cases early and can separate them into the types which I have endeavored to make clear much can be done in an abortive way. My best results have been obtained in what I will term the hemorrhagic type, by rest in bed, free catharsis, leeching in front of the tragus and over the mastoid, and hot douching of the canal every two hours. I do not here incise the membrane. The writer is well aware that this method of hot douching has been severely criticised, and it is said the tissues macerate, making perforation more liable; but in my hands this has not been the case, and I have found that it has given me the largest percentage of recoveries. These are the cases wherein I feel we are justified in applying abortive measures. It is my impression that in this variety of acute otitis we have the same condition of

the mucous membrane of the antrum and possibly the cells that we find in the tympanum. Whether my impression be true or erroneous, a considerable number of these cases recover under abortive treatment, be it ice-bag, heat, or leeching.

In the other variety, or that of grippal infection with suppuration, the writer is equally radical, as he would appear conservative in the hemorrhagic variety. From the fact that suppurative influenza otitis almost always runs an acute course up to the inception of the dangerous complications, and being convinced that the antrum is early invaded by the suppurative process and, in rapid succession, the mastoid cells, I do not feel justified in prolonging conservative treatment. Early and free incision of the drum membrane, warm douching every two hours for cleansing purposes, rest, and catharsis, constitute my early treatment. In my experience if this does not yield palpable results in thirty-six to forty-eight hours the case will be one for surgical interference. To prolong conservative measures is to jeopardize the welfare of our patient. The writer is convinced that it is not a wise plan to apply the ice-coil in any case where the mastoid is involved in a purulent inflammation, from the fact that it will mask the symptoms and lead us astray in estimating the extent of the process, and before it is realized our patient is beyond the border-line of safety. I think each one of us, in operating early on acute cases, must have been surprised to find the amount of destruction which had taken place in so short a time. I have seen the entire mastoid in a purulent and necrotic condition, with involvement of the facial nerve and complete facial paralysis, in one week from the first ear symptoms. It is generally agreed that a pyogenic disease of the mastoid is a dangerous condition; therefore, if we feel satisfied that such exists it is, I believe, our duty to immediately open the mastoid cells and not try to palliate or abort an already dangerous condition. In those cases where we are in doubt and where conservative treatment has proved inefficient, it would seem that an exploratory operation, spoken of by Dench at our recent annual meeting, would be justifiable. The operation, *per se*, is practically devoid of danger in the hands of an ordinarily skilful operator, and aside from the cosmetic effect I can see no valid objection to it.

In conclusion, I wish to emphasize the fact that in influenza we get two distinct types of tympano-mastoiditis: First, the suppurative, which invades the tympanum, antrum, and cells almost simultaneously in an unusually virulent and destructive process, which calls for early surgical treatment and in which abortive measures are contraindicated. Second, the hemorrhagic, with very pronounced symptoms at first, but which yields readily to abortive measures, and, in the writer's experience, only about 5 per cent. go on to suppuration requiring radical interference.

A METHOD FOR THE DIFFERENTIAL MODIFICATION OF THE PROTEIDS IN PERCENTAGE MILK MIXTURES.

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In a monograph on "The Scientific Modification of Milk," recently published (*International Clinics*, October, 1900), the writer has given numerous formulæ for calculating the proportions of the various milk-derived fluids required in making percentage mixtures. These include combinations of cream and whole milk, cream and separated (fat-free) milk, gravity cream and its separated (under) milk, cream and whey, and simple cream dilutions.

In all these combinations, except indirectly in the all-cream-and-whey mixtures, the total proteids alone are considered in working out the modified proteid percentage, and thus the relative proportions of lactalbumin and caseinogen that are found in the basal milk and cream are not susceptible of variation in these ordinarily employed modifications. In the cream and whey mixtures, which are made by diluting creams of various fat percentage with pure whey, the proportion of lactalbumin is considerably increased as compared with that obtained in the other milk combinations containing the same total proteid percentage; but until recently no means of obtaining definite percentages of lactalbumin and caseinogen has been devised.

A preliminary note upon such a method was communicated by the writer to the Philadelphia Pediatric Society at its meeting in October, 1900. About the same time the problem was undertaken by the Walker-Gordon Laboratory Company, following the experimental work of Franklin W. White and Maynard Ladd, of Boston, who have given a partial exposition of the subject in a valuable paper of recent date (*Philadelphia Medical Journal*, February 2, 1901). In this communication the possibilities of the method are touched upon, but no definite rules for its practical application are suggested. The object of the present paper, therefore, is to describe a simple method for obtaining definite percentages of lactalbumin and caseinogen in combination with definite fat and sugar percentages.

One of the great difficulties in artificial feeding with ordinary milk and cream mixtures lies in the large proportion of caseinogen that must be given to the infant in order to provide a sufficiently rich proportion of the proteid elements. The writer has elsewhere shown[1] that satisfactory nutrition in a child, aged three or four months, cannot be

[1] "The Scientific Modification of Milk," International Clinics, October, 1900, p. 266.

expected from a mixture containing less than 1.50 per cent. of combined proteids, and by a simple calculation it can readily be proven that in the ordinary milk and cream dilutions containing this percentage of proteids, fully 1.20 per cent. consists of caseinogen, just about twice as much as is found in human milk, to say nothing of physical differences in this body as it exists in cow's milk, which render it much less readily digestible by the human suckling than is human caseinogen.

Again, the analysis of human milk proteids shows an average percentage of only 0.59 caseinogen with fully 1.23 lactalbumin (Koenig), while cow's milk contains at least 2.48 per cent. caseinogen with only 0.66 per cent. lactalbumin (Van Slyke). This large excess of lactalbumin over caseinogen in human milk naturally suggests that the former proteid body is much more important for the needs of the growing infant than is the caseinogen, which forms less than one-third the total proteid percentage. It is, therefore, evident that if the analysis of mother's milk is to be used as a standard for the composition of milk mixtures for the artificial feeding of young infants, account must be taken of this wide divergence in the proportions of the two principal proteid bodies in the cow's milk.

Any dilution of cow's milk that brings the caseinogen percentage down to a figure corresponding with that found in human milk (0.59), say one part of milk to four parts of water, reduces at the same time the lactalbumin percentage of the mixture to something like 0.13, about one-tenth of the amount found in the human breast secretion. If, then, lactalbumin must be considered an important element of the breast milk proteids, such a reduction of its percentage in an artificial mixture constitutes a grave defect in the ordinary methods of modification based simply upon a reduction of the total proteid percentage.

Even in a mixture in which the total proteids are made about 1.50 per cent. the percentage of lactalbumin would be only 0.30, a proportion which is still but a fourth of the normal lactalbumin percentage of mother's milk, while, as has already been shown, the caseinogen percentage is still twice as large as the normal.

It is quite possible that in certain cases in which breast milk produces indigestion in the nursing infant some change in the relative proportion of caseinogen may be at fault, and may constitute one of the alterations to which we rather vaguely apply the term "disturbance of equilibrium." If it were possible definitely to modify this percentage for the individual case maternal feeding might be kept up when otherwise it becomes necessary to wean the infant from what in other respects appears to be a desirable maternal supply. This, it must be confessed, is a purely theoretical suggestion upon which no definite analytical investigation has been carried out, but it serves to emphasize the importance of greater flexibility than has been previously afforded for

the delicate manipulation of the proteid percentages in artificial feeding, with which at present we are exclusively concerned.

It is thus made manifest that a simple cream, milk, and water mixture, in which total proteids alone are considered, does not fulfil the demand for wider latitude in a regulation of caseinogen and lactalbumin percentages, and that another milk-derived fluid is needed to permit of increase in the deficient lactalbumin percentage, just as cream serves to raise the unduly low percentage of fat resulting from dilution. Such a fluid is whey, which contains fully 1.00 per cent. of proteids other than caseinogen, the latter having been removed from the milk in the process of whey preparation. Whey has always occupied a place in infant diet, but its possibilities have as yet attracted little attention in modern methods of feeding, except in the writings of Kehrer and very recently in those of Monti.[1] Its proteids consist almost entirely of lactalbumin, with a very small proportion of lactoglobulin, and perhaps other soluble proteids in minute quantities. These bodies collectively have been termed the whey-proteids by White and Ladd (*loc. cit.*). The term, however, is rather awkward, and, since lactalbumin forms almost the entire proteid content of the whey, it seems best to speak of the whey-proteids specifically as lactalbumin, and as such the term will be hereafter used.

There is thus presented the problem of combining cream, milk, whey, sugar of milk and a diluent in such proportions as to furnish definite percentages of fat, caseinogen, lactalbumin, and sugar within the limits of practical possibility.

The keynote of such a modification is to be found in the ratio existing in cow's milk between the normal percentages of caseinogen and lactalbumin. According to Koenig's well-known analyses, which give 2.88 per cent. caseinogen to 0.53 lactalbumin, this ratio is seen to be nearly 5½ to 1. White and Ladd (*loc. cit.*) have essayed to establish a new ratio between caseinogen and whey-proteids obtained from the milk of the Walker-Gordon Laboratory of Boston, and in several analyses found that the total proteids averaged 3.84 per cent., of which 0.90 per cent. was whey-proteids and 2.94 per cent. caseinogen. This average of analysis, it will be observed, gives the percentage of total proteids of whole milk considerably higher than that usually obtained, with a percentage of whey-proteids far beyond that of any other analysis with which the writer is familiar in the literature. It is also noteworthy that the percentage of total proteids in the Boston milk is considerably higher than that obtained by Leffmann in Walker-Gordon milk from the Plainsboro dairy, the percentage of which for nine months has averaged about 3.3 (statistics Pediatric Society Milk Commission). The ratio between caseinogen and whey-proteids thus

[1] Archiv f. Kinderheilk., Bd. xxxi., Heft 1 und 2.

deduced by White and Ladd is therefore about 3 to 1; and it is to be presumed that upon this ratio the laboratory has based the calculations for its so-called whey-cream modifications, which, according to these investigators, are made from 32 per cent. cream, fat-free milk, fat-free whey, and a very concentrated solution of milk sugar.

An examination of the literature shows that in 1893 Van Slyke (*Journal of the American Chemical Society*, November, 1893, p. 605) reached the following conclusion: That in analyses of whole milk the caseinogen has varied from 1.93 to 3, and averages 2.48; that the albumin has varied from 0.55 to 0.86, and has averaged 0.66 per cent. This percentage for the lactalbumin also agrees very closely with that given by Blyth (*Foods: Composition and Analysis*, second edition, p. 208), who asserts that the albumin is quite fairly constant and averages 0.70. Van Slyke states that milk rarely contains five parts of casein to one of albumin, and not often does the ratio go above 4½ to 1, and seldom goes below 3 to 1, while the average is somewhat under four parts to one. This proportion also agrees very closely with the estimation previously made by Leeds.

We have thus a rather varied estimation of this important ratio, ranging from Koenig's 5½ to 1, to Van Slyke's and Leeds' 4 to 1, down, finally, to White and Ladd's 3 to 1. Since White and Ladd's ratio of 3 to 1 is based upon what they speak of as "several analyses" only, it would seem more satisfactory for the present to use Van Slyke's average ratio of 4 to 1, which is based upon a considerable number of analyses of milk from American dairies.

A feature of decided interest brought out by White and Ladd's study is the fact that whey contains about 1.00 per cent. proteids, which is slightly higher than Koenig's estimate of 0.86 per cent. This higher figure, too, agrees with analyses published by the United States Department of Agriculture, which, as the mean of a large number of analyses of whey, gave a whey-proteid percentage of 1.00. White and Ladd have suggested that the whey should be made from fat-free milk, and they have thus obtained a fluid containing no fat with 1.00 per cent. of lactalbumin and about 4.8 per cent. sugar. This suggestion is of special value since, in the first place, it decidedly simplifies the somewhat tedious calculations necessitated by the use of a whey containing a small percentage of fat, and, in the second place, it makes for economy in permitting the use of fat-free milk, which in a way is a waste-product of the dairy, and can be obtained from the laboratory at a very moderate cost.

The modification which is now to be described is made from cream (usually 16 per cent., sometimes 20 per cent., and very rarely 32 per cent.), whole milk, fat-free whey, and a diluent, or from various combinations of two or three of these fluids, to which is to be added the

amount of sugar in dry form required to bring up the sugar percentage, and, if desired, lime-water to produce the necessary alkalinity. It is quite evident that when all three milk-fluids are combined the fat of the finished mixture will be supplied by the cream and the milk, the caseinogen by the cream and the milk, and the lactalbumin by the cream, by the milk, and, usually in greatest part, by the whey. Sugar is contributed by all three of these milk-fluids, and by the added sugar of milk.

It will be observed that the milk and the cream supply all the caseinogen and a portion of the lactalbumin. The proportion of lactalbumin thus supplied must bear the normal ratio to the amount of caseinogen, or, in other words, the milk and cream supply the desired caseinogen percentage plus a portion of the desired lactalbumin percentage equal to one-fourth of the caseinogen percentage. The balance of the lactalbumin percentage, if any remain to be added, will therefore be furnished by the whey. The practical problem thus becomes quite a simple one.

Calculation of Formulæ. The following symbols will be used in the calculations:

F = the desired fat percentage.		C = quantity of cream in ounces.	
K = " caseinogen per ct.		M = " milk "	
A = " lactalbumin "		Wh = " whey "	
S = " sugar "		L = " dry sugar of milk in ounces.	
		W = " diluent "	
		Q = " total mixture "	

To these are to be added two intermediate values:

P′ = percentage of combined proteids supplied by milk and cream.
A′ = " of lactalbumin supplied by whey.

The first step is to derive values for P′ and A′. These are readily found, since we know that the milk and cream furnish all the caseinogen percentage plus a part of the lactalbumin percentage equal to one-fourth of the caseinogen percentage; and the percentage of lactalbumin to be furnished by the whey is what remains after deducting from the total desired lactalbumin percentage the percentage already supplied by the milk and cream. We thus find:

(1) $$P' = K + \tfrac{1}{4} K$$

(2) $$A' = A - \tfrac{1}{4} K$$

Having found the value of A′, the quantity of whey is very simply calculated by the proportion A′ : 1.00 : : Wh : Q, whence the equation:

(3) $$Wh = \frac{A'}{1.00} \times Q = A' \times Q$$

The quantities of milk and cream are next found by substituting P′ for P in the regular formulæ :[1]

$$(4) \qquad C = \frac{(F - P')Q}{12.4 \text{ or } 16.8 \text{ or } 29.2}$$

$$(5) \qquad M = \frac{Q \times F}{4} - 4 \text{ or } 5 \text{ or } 8 \times C$$

The quantity of diluent will be found by subtracting from the total quantity of mixture the combined sum of the quantities of cream, milk, and whey, thus :

$$(6) \qquad W = Q - (C + M + Wh)$$

The formula for sugar gives the amount of dry sugar of milk in ounces to be added :

$$(7) \qquad L = \frac{Q \times S - (4\,C + 4.4\,M + 4.8\,Wh)}{100}$$

For the sake of simplicity this formula may be expressed with sufficient accuracy :

$$L = \frac{Q \times S - 4.4\,(C + M + Wh)}{100}$$

In the modifications suggested by White and Ladd a 32 per cent. cream is used in combination with a separated (fat-free) milk. This is quite feasible in the laboratory, but for home modification so rich a cream cannot easily be obtained, and is generally unnecessary when whole milk instead of separated milk is used in combination with it. For the ordinary combinations a 16 per cent. cream will be found sufficiently rich. It is only when the milk formula (5) works out a negative value that a higher fat cream is required, and for the majority of such formulæ a 20 per cent. cream will be found rich enough.

If, however, it is desired to make the modification with fat-free milk instead of whole milk, formulæ (4) and (5) become :[2]

$$(4') \qquad C = \frac{Q \times F}{16 \text{ or } 20 \text{ or } 32}$$

$$(5') \qquad M = \frac{Q \times P' - (3.6 \text{ or } 3.2 \text{ or } 2.8)\,C}{4}$$

In these formulæ, 16 and 3.6, or 20 and 3.2, or 32 and 2.8 are to be taken as 16, 20, or 32 per cent. cream is used.

One or two examples will show how readily these calculations can be made.

[1] For an explanation of the derivation of formulæ (4), (5), and (7), the reader is referred to the author's monograph on the subject (International Clinics, November, 1900, p. 233). When 16 per cent. cream is used the divisor in (4) is 12.4, and the coefficient of C in (5) is 4. When 20 per cent. cream is required 16.8 and 5 respectively are to be used ; and with 32 per cent. cream 29.2 and 8 are similarly to be chosen.

[2] International Clinics, November, 1900, p. 256.

Example I. Required the proportions of whole milk, 16 per cent. cream, whey, and sugar to give a modified formula containing fat, 3.50; caseinogen, 0.80; lactalbumin, 0.50, and sugar, 6.00 in a total mixture of forty ounces.

Here (1) becomes

$$P' = 0.80 + 0.20 = 1.00$$

and (2)

$$A' = 0.50 - 0.20 = 0.30$$

Therefore, we obtain at once from (3)

$$Wh = 0.30 \times 40 = 12 \text{ oz.}$$

By substituting in (4) the value obtained for P′ we get

$$C = \frac{(3.50 - 1.00)\ 40}{12.4} = 8 \text{ oz.},$$

and, therefore,

$$M = \frac{3.50 \times 40}{4} - 4 \times 8 = 35 - 32 = 3 \text{ oz.}$$

The quantity of diluent is found by substituting these values in (6):

$$W = 40 - (8 + 3 + 12) = 17 \text{ oz.}$$

The quantity of dry sugar of milk to be dissolved in the diluent before combining the ingredients is found by substituting in (7):

$$L = \frac{40 \times 6 - (4 \times 8 + 4.4 \times 3 + 4.8 \times 12)}{100} = \frac{240 - 102.8}{100} = 1\tfrac{3}{8} \text{ oz.}$$

The modification would, therefore, be made after the following recipe:

Cream 16 per cent.	8 oz.
Milk	3 "
Whey	12 "
Diluent	17 "
Dry sugar of milk	$1\frac{3}{8}$ "

If desired, lime-water may be added to produce an alkaline reaction in the proportion of 5 to 10 per cent. of the mixture. Thus two to four ounces of the diluent may be replaced by an equal quantity of lime-water.

If separated milk were used in place of whole milk we should have from (4′) and (5′):

$$C = \frac{40 \times 3.50}{16} = 8\tfrac{3}{4} \text{ oz.}$$

$$M = \frac{40 - 31.5}{4} = 2\tfrac{1}{8} \text{ oz.}$$

The quantity of whey would remain the same as in the previous example, since the value of A′ would not be affected by variations in the values of C and M.

Example II. Required the proportions of 16 per cent. cream, whole milk, whey, and sugar to give a modified formula of forty ounces containing fat, 3.00; caseinogen, 0.40; lactalbumin, 0.75; sugar, 6.50.

Here, as before, we obtain:

$$P' = 0.40 + 0.10 = 0.50$$

$$A' = 0.75 - 0.10 = 0.65$$

Therefore,

$$Wh = 0.65 \times 40 = 26 \text{ oz.}$$

$$C = \frac{(3 - 0.50)\,40}{12.4} = 8 \text{ oz.}$$

$$M = \frac{3 \times 40}{4} - 4 \times 8 = -2 \text{ oz.}$$

This result shows that a 16 per cent. cream contains too low a proportion of fat, and, therefore, a higher-fat cream must be used. A 20 per cent. cream will serve the purpose, and thus using 16.8 as a divisor in (4) and 5 instead of 4 as a coefficient of C in (5) we obtain:

$$Wh = 0.65 \times 40 = 26 \text{ oz.}$$

$$C = \frac{(3 - 0.50)40}{16.8} = 6 \text{ oz.}$$

$$M = \frac{3 \times 40}{4} - 5 \times 6 = 0.$$

$$L = \frac{40 \times 6.50 - 4 \times 6}{100} = 2\tfrac{3}{4} \text{ oz.}$$

and

$$W = 40 - (26 + 6) = 8 \text{ oz.}$$

Practical Limitations of this Modification. It is quite evident that in any mixture containing whey the percentage of lactalbumin could not exceed 1.00, and could never quite reach this figure, since cream or milk added to the mixture to supply fat would have the effect of diluting the whey and thus reducing the lactalbumin percentage below 1.00. This loss could not be entirely made good by the added milk or cream, since the lactalbumin percentage of milk or cream is only one-fifth of its total proteids.

It is therefore important to determine the limits within which caseinogen and lactalbumin percentages may be modified. In the first place, the lowest possible percentage of lactalbumin will be obtained when A′ is equal to 0, which is seen to be the case when $A = \frac{1}{4} K$. It is also evident that the lowest possible caseinogen percentage will be obtained when the ratio between fat and caseinogen is such as to require only cream and no milk in the modification. By taking a value for P′ in terms of K from (1), we obtain:

$$(8) \qquad P' = \frac{5K}{4}$$

This value of P′ may now be substituted for P in a formula representing the relation between P and F in a mixture containing 16 per cent. cream and no milk :[1]

$$P = 0.225\,F, \tag{9}$$

and we obtain

$$\frac{5K}{4} = 0.225\,F,$$

or

$$5K = 0.90\,F;$$

and

$$K = 0.18\,F; \tag{10}$$

and therefore

$$A = 0.045\,F. \tag{11}$$

It thus becomes evident that the lowest possible percentages of caseinogen and lactalbumin are conditioned by the percentage of fat desired. For example, when the fat percentage is 3.00 the lowest caseinogen percentage will be $0.18 \times 3 = 0.54$, and the lowest lactalbumin percentage will be $0.045 \times 3 = 0.135$. Such a formula should work out as a simple cream dilution, without milk or whey; thus, for forty ounces :

$$P' = 0.54 + 0.135 = 0.675$$

$$A' = 0.135 - 0.135 = 0.$$

$$Wh = 0 \times 40 = 0.$$

$$C = \frac{(3 - 0.675)\,40}{12.4} = 7\tfrac{1}{2} \text{ oz.}$$

$$M = \frac{40 \times 3}{4} - 4 \times 7\tfrac{1}{2} = 0.$$

If a 20 per cent. cream be used we may substitute the value of P′ from equation (8) in the formula expressing the relation between F and P in 20 per cent. cream dilutions :[2]

$$P = 0.16\,F; \tag{12}$$

and we obtain

$$\frac{5K}{4} = 0.16\,F,$$

$$5K = 0.64\,F,$$

and

$$K = 0.128\,F; \tag{13}$$

and therefore

$$A = 0.032\,F. \tag{14}$$

Thus, for 3 per cent. fat the lowest possible caseinogen percentage from 20 per cent. cream is $0.128 \times 3 = 0.384$, and the lowest lactalbumin percentage is $0.032 \times 3 = 0.096$.

In like manner, for 32 per cent. cream the minimal values for K and A for any percentage of fat are found to be :

$$K = 0.07\,F, \tag{15}$$

$$A = 0.0175\,F; \tag{16}$$

and thus for 3 per cent. of fat the minimum caseinogen percentage is 0.21 and the minimum lactalbumin percentage is 0.0525.

[1] For derivation of formulæ (9), (12), and (15), the reader is referred to the author's monograph, p. 253.

[2] Ibid.

Starting from such minimum percentages of caseinogen and lactalbumin in simple cream dilutions, increasing values may be obtained as milk and whey are added to the mixture.

The maximum value for caseinogen would be reached when both forms of proteid were furnished by milk without additional cream, the quantity of milk, and consequently the caseinogen percentage, being conditioned as before by the fat percentage. This would obtain when the value of C in formula (4) becomes 0, which requires that

$$F = P'.$$

By substituting here the value of P′ from (8) we obtain:

or
$$F = \frac{5K}{4},$$

(17)
$$K = 0.80\,F.$$

This signifies that for any fat percentage the maximum caseinogen percentage is four-fifths as great; thus for 3 per cent. fat the maximum caseinogen percentage is 2.40.

The maximum lactalbumin percentage that may be combined with a maximum caseinogen percentage for any definite fat percentage will be obtained when whey without additional water forms the diluent, the total percentage of caseinogen being furnished by whole milk. This condition is expressed by the equation:

$$Wh = A'Q = Q - M.$$

Referring to formula (6) it will be seen that when C is 0 the equation for milk becomes:

$$M = \frac{QF}{4}.$$

This value for M, substituted above, gives:

$$A'Q = Q - \frac{QF}{4},$$ whence by dividing out Q,

$$A' = 1 - \frac{F}{4};$$ and by substituting the value of

A′ from (2)
$$A - \frac{K}{4} = 1 - \frac{F}{4},$$

or (18)
$$A = 1 - \frac{F}{4} + \frac{K}{4},$$

which expresses the maximum value of A for any value of F which determines a maximum value for K. If the value of K in terms of F, as derived from (17), be substituted, we obtain finally:

(19)
$$A = 1 - \frac{F}{4} + \frac{F}{5} = 1 - 0.05\,F.$$

Thus under the conditions of the problem it is evident that the maximum value for the lactalbumin percentage when F is 1.00 and K is a maximum is 0.95; when F is 2.00, it is 0.90; when F is 3.00, it is 0.85, and when F is 4.00, it is 0.80.

It is quite obvious that when K is less than a maximum for any definite fat percentage the lactalbumin percentage may be slightly higher than the figures just given, since a somewhat larger amount of whey could be used to make up for the decrease in the quantity of milk and cream required to give a lower than a maximum caseinogen percentage. The maximum limit of the lactalbumin percentage under these conditions will be attained when all the diluent is whey, which thus is equal to $Q - (M + C)$.

By a similar but considerably more complicated calculation than that by which (19) is derived, we can finally deduce for 16 per cent. cream and whole milk mixtures:

$$A = 1 - 0.0524\,K - 0.008\,F; \tag{20}$$

for 20 per cent. cream,

$$A = 1 - 0.0476\,K - 0.012\,F; \tag{21}$$

and for 32 per cent. cream,

$$A = 1 - 0.0496\,K - 0.010\,F, \tag{22}$$

each of which expresses, for the strength of cream used the maximum value for the lactalbumin percentage for any definite fat and caseinogen percentage. The results obtained by working out these values of A for definite fat values when minimal values for K are used, show that the possible maximal lactalbumin percentage can be increased above that possible for maximal caseinogen values by quantities varying from 0.03 at the lower end of the scale to 0.11 at the upper limit. This, of course, is only possible when there is no watery diluent. Since, however, a small quantity of water is useful in dissolving the additional sugar of milk, which does not dissolve readily in the milky fluids, it is preferable to restrict the lactalbumin percentages to something less than those that can be obtained theoretically. For practical purposes the figures given in the last column of the following table, which are only possible with the minimum caseinogen percentages, may be slightly reduced to those given in the third column as obtainable with maximum caseinogen percentages, and these latter can always be obtained with any caseinogen percentage between the minimum and maximum values. Thus, for 3 per cent. of fat, lactalbumin percentages between 0.06 and 0.85 may be obtained with any possible caseinogen percentage, the limits of which are given in the second column of the table (0.21 to 2.40), provided, always, that the desired lactalbumin percentage shall not fall below one-fourth of the caseinogen percentage.

TABLE SHOWING THE MAXIMUM AND MINIMUM VALUES OF PERCENTAGES OF CASEINOGEN AND LACTALBUMIN OBTAINABLE WITH ANY DEFINITE FAT PERCENTAGE.

Fat percentage.	Range of possible caseinogen percentages.	Range of possible lactalbumin percentages.	Maximum lactalbumin percentage for minimum caseinogen percentage.
1.00	0.18 (16 per ct.) 0.128 (20 ") } to 0.80 0.07 (32 ")	0.045 (16 per ct.) 0.032 (20 ") } to 0.95 0.0175 (32 ")	0.98 0.98 0.98
1.25	0.225 (16 ") 0.16 (20 ") } to 1.00 0.0875 (32 ")	0.056 (16 ") 0.040 (20 ") } to 0.93 0.0218 (32 ")	0.97 0.97 0.98
1.50	0.27 (16 ") 0.192 (20 ") } to 1.20 0.105 (32 ")	0.0675 (16 ") 0.048 (20 ") } to 0.92 0.0262 (32 ")	0.97 0.97 0.97
1.75	0.315 (16 ") 0.224 (20 ") } to 1.40 0.1225 (32 ")	0.0787 (16 ") 0.056 (20 ") } to 0.91 0.0306 (32 ")	0.96 0.96 0.97
2.00	0.36 (16 ") 0.256 (20 ") } to 1.60 0.140 (32 ")	0.09 (16 ") 0.064 (20 ") } to 0.90 0.035 (32 ")	0.96 0.96 0.97
2.25	0.405 (16 ") 0.288 (20 ") } to 1.80 0.1575 (32 ")	0.10125(16 ") 0.072 (20 ") } to 0.88 0.039 (32 ")	0.96 0.95 0.96
2.50	0.45 (16 ") 0.32 (20 ") } to 2.00 0.175 (32 ")	0.1125 (16 ") 0.080 (20 ") } to 0.87 0.04375(32 ")	0.95 0.95 0.96
2.75	0.495 (16 ") 0.352 (20 ") } to 2.20 0.1925 (32 ")	0.12375(16 ") 0.088 (20 ") } to 0.86 0.04812(32 ")	0.95 0.95 0.96
3.00	0.54 (16 ") 0.384 (20 ") } to 2.40 0.21 (32 ")	0.135 (16 ") 0.096 (20 ") } to 0.85 0.0525 (32 ")	0.94 0.94 0.95
3.25	0.585 (16 ") 0.416 (20 ") } to 2.60 0.2275 (32 ")	0.14625(16 ") 0.104 (20 ") } to 0.83 0.05687(32 ")	0.94 0.94 0.95
3.50	0.63 (16 ") 0.448 (20 ") } to 2.80 0.245 (32 ")	0.1575 (16 ") 0.112 (20 ") } to 0.82 0.06125(32 ")	0.93 0.94 0.95
3.75	0.675 (16 ") 0.480 (20 ") } to 3.00 0.2625 (32 ")	0.16875(16 ") 0.120 (20 ") } to 0.81 0.06565(32 ")	0.93 0.93 0.94
4.00	0.72 (16 ") 0.512 (20 ") } to 3.20 0.28 (32 ")	0.18 (16 ") 0.128 (20 ") } to 0.80 0.07 (32 ")	0.93 0.92 0.94

A glance at this table will show the limits within which differential modification of proteids is possible. For example, a mixture containing 2.50 fat, 1.00 caseinogen, and 0.50 lactalbumin can be worked out by the formulæ already given, but the same combination of fat and caseinogen with only 0.20 lactalbumin could not be obtained, since the lactalbumin is less than one-fourth of the caseinogen. If 0.25 lactalbumin be chosen, the problem becomes a possible one.

From the various hypotheses just made in working out maximum and minimum values it appears that these mixtures may consist of simple cream dilutions; cream, milk, and water; cream, whey, and water; milk and water; milk, whey, and water; cream and whey; milk and whey; cream, milk, and whey; and cream, milk, whey, and water, any one of which may be required according to the relative percentages of fat, caseinogen, and lactalbumin demanded in the modification. The use of separated (fat-free) milk is also possible in certain cases in combination with cream, with cream and whey, or with cream, whey, and water.

Reasoning conversely, it becomes evident that any of these various combinations of the milk fluids must contain definite percentages of fat, caseinogen, lactalbumin, and sugar; and it is possible to accurately estimate in any mixture of known proportions of these fluids just what the various percentages are. The following formulæ are necessary:

(23) For fat percentage

$$\begin{cases} \frac{C}{Q} \times (16 \text{ or } 20 \text{ or } 32)^* = \text{fat percentage from cream.} \\ \frac{M}{Q} \times 4 = \text{fat percentage from milk.} \end{cases}$$

Sum of these = fat percentage in modification.

(24) For caseinogen percentage

$$\begin{cases} \frac{C}{Q} \times (3.6 \text{ or } 3.2 \text{ or } 2.8)^* \times \frac{4}{5} = \text{caseinogen per ct. from cream.} \\ \frac{M}{Q} \times 4 \times \frac{4}{5} = \text{caseinogen percentage from milk.} \end{cases}$$

Sum of these = caseinogen percentage in modification.

(25) For lactalbumin percentage

$$\begin{cases} \frac{C}{Q} \times (3.6 \text{ or } 3.2 \text{ or } 2.8)^* \times \frac{1}{5} = \text{lactalbumin per ct. from cream.} \\ \frac{M}{Q} \times 4 \times \frac{1}{5} = \text{lactalbumin percentage from milk.} \\ \frac{Wh}{Q} \times 1 = \text{lactalbumin percentage from whey.} \end{cases}$$

Sum of these = lactalbumin percentage in modification.

A similar calculation would give the sugar percentage of the modification without taking into account the added sugar, or, if this latter be desired, a formula may be derived from (7) by transposition:

$$(26) \qquad S = \frac{100\,L + 4\,C + 4.4\,M + 4.8\,Wh}{Q}$$

This method of modification, therefore, covers the whole range of modified milk mixtures, and effects a definite modification of fat, caseinogen, lactalbumin, and sugar within possible limits—a very decided advance over any method that hitherto has been proposed either in laboratory or in home modification.

* One or other of these factors is to be taken as 16 per cent., 20 per cent., or 32 per cent. cream is used, 16 and 3.6, 20 and 3.2, or 32 and 2.8, respectively, being required.

Practical Application of these Modifications. In practice the use of mixtures prepared under this system of modification has yielded the most gratifying results, especially with cream and whey, or milk and whey, or cream, whey, and water, or cream, milk, whey, and water combinations. In the most difficult cases, in which very low percentages of caseinogen are at first required, these combinations may be used in a sort of progressive series, beginning with a cream, whey, and water, or a cream and pure whey mixture. Then by a gradual increase of the caseinogen percentage secured by adding successive small quantities of milk, while the whey or water is decreased equally so as to preserve a constant total quantity of the mixture, the combination becomes one of cream, milk, and whey, or cream, milk, whey, and water; and if the decrease is confined to the whey alone, or if at the time the milk is increased the water is also increased while the whey alone is decreased, we after a time reach a point when the quantity of whey becomes so small, say six to eight ounces, that it may be omitted altogether, its bulk being supplied by the same quantity of water. Thus the mixture becomes a simple cream, milk, and water modification, from which, by continued increase of milk, decrease of water, and, after the fat percentage reaches 4.00, by appropriate decrease of the cream, we finally reach whole milk.

To put this in a concrete example, let us suppose by aid of the table we begin with a formula of fat, 2.00; caseinogen, 0.36; lactalbumin, 0.50 (total proteids, 0.86), and sugar, 5.00. This should require cream, whey, and water, the quantities of which for a forty-ounce mixture will be found to be cream (16 per cent.) five ounces; whey, sixteen and two-fifth ounces; water, eighteen and three-fifth ounces, and sugar of milk, one ounce. If this mixture is found to be well digested an effort may be made to increase the caseinogen percentage. This may be done in one of two ways: either a new formula may be calculated, say for 0.40 per cent. caseinogen, the other percentages being left as before, or a more complex change may be made by adding a small quantity of milk, which will slightly increase not only the caseinogen percentage, but also those of the fat, lactalbumin, and sugar. In general, an increase in all the percentages is desirable, especially when the initial formula has been made low in all its percentages. In the example the addition of a half-ounce of milk, with the decrease of a half-ounce in the quantity of water, will be found to add 0.05 per cent. to the fat, 0.04 per cent. to the caseinogen, 0.055 per cent. to the sugar, and 0.01 per cent. to the lactalbumin. The new mixture will, therefore, contain cream, five ounces; milk, one-half ounce; whey, sixteen and two-fifth ounces; water, eighteen and one-tenth ounces, and sugar of milk, one ounce, and its percentage equivalent will become: F 2.05; K 0.40; A 0.51, and S 5.055.

Of the two plans the latter is much to be preferred, since it permits frequent changes to be made without a recalculation of the quantities, and thus the mother can be given general instructions and can continue to increase the percentages of the formula without constant supervision. Suppose in this way she has gradually added milk and decreased water until her working formula stands: cream, five ounces; milk, ten ounces; whey, sixteen and two-fifth ounces; water, eight and three-fifth ounces, and sugar of milk, one ounce. By means of formulæ (23), (24), and (25) it can be readily calculated that the percentage formula has now become: F 3.00; K 1.16; A 0.70 (total proteids, 1.86), and S 6.10—a very nutritious mixture differing little from that of a good average breast milk, except in the relative proportions of caseinogen and lactalbumin. A closer imitation could be made, if desired, by reducing the percentage of caseinogen and increasing that of lactalbumin, say caseinogen 0.96 and lactalbumin 0.90, which a glance at the table shows to be a possible combination.

In the formula as it now stands (F 3.00; K 1.16; A 0.70, and S 6.10) the lactalbumin percentage contributed by the whey—0.41—is rather too important to be sacrificed at this point, since the total proteid percentage without it would fall to 1.45, and we shall, therefore, continue for a time to increase the milk and decrease the water; or, if it is desirable as quickly as possible to get rid of the necessity of preparing whey, the water may be kept at eight and three-fifth ounces, and the whey alone may be decreased step by step with the increase of the milk.

By this plan the quantity of whey will be decreased while the lactalbumin percentage suffers little change, as can be shown: the increase of an ounce of milk will add 0.10 per cent. to the total proteids (or 0.08 to the caseinogen and 0.02 to the lactalbumin), while the decrease of an ounce in the quantity of whey will take away only 0.025 from the lactalbumin, and thus the total lactalbumin percentage will be scarcely disturbed. Under this plan the addition of eight ounces of milk, with an equal decrease of whey, will add 0.80 per cent. to the total proteids, or 0.64 per cent. caseinogen, and 0.16 per cent. lactalbumin; while the decrease of eight ounces of whey will subtract 0.20 per cent. lactalbumin, leaving the total lactalbumin at 0.66 per cent., only 0.04 below the previous formula. At this point the remaining eight and two-fifth ounces of whey, which contribute only 0.21 per cent. lactalbumin, may be omitted, its bulk being replaced by simple diluent. We have thus reached by gradual steps a cream, milk, and water modification of the ordinary kind, consisting of cream, five ounces; milk, eighteen ounces; water, seventeen ounces, and sugar, one ounce, containing these percentages: F 3.80; K 1.80; A 0.45 (total proteids, 2.25); and S about 5.00, the withdrawal of the whey,

which is rich in sugar, having decreased the sugar percentage from 6.10. If so desired this percentage may be increased by the addition of a quantity of sugar of milk to be determined by formula (7).

Starting, now, from the cream, milk, and water combination, containing cream, five ounces; milk, eighteen ounces, and water, seventeen ounces, the milk may be gradually increased until two ounces more are added to the milk and two ounces taken from the water. At this point the fat percentage becomes 4.00, which is as high as it is generally desirable to have it. Subsequent increase of the milk may be associated with a decrease of the cream, one drachm of 16 per cent. cream being omitted for each half-ounce of milk added, or one drachm of 20 per cent. cream for five drachms of milk. By this device the fat is kept at about 4 per cent., while the proteid percentage goes on increasing until, when finally the quantity of milk reaches forty ounces, the cream and water have been replaced entirely by milk and the mixture becomes unmodified whole milk.

This example shows one of many possible methods of varying the relative proportions of caseinogen and lactalbumin in feeding a single case. If evidences of casein indigestion should appear in the stools the caseinogen percentage may be decreased, while the fat and lactalbumin percentages are varied according to indications. For example, by reference to the table, it will be seen that for 2 per cent. fat a caseinogen percentage as low as 0.14 may be obtained by using a 32 per cent. cream, and that even with a 16 per cent. cream the caseinogen percentage may be kept as low as 0.36. With this latter very low caseinogen percentage any lactalbumin percentage from 0.09 up to 0.96 per cent. may be obtained, a resulting total of 1.32 per cent. of mixed proteids for the maximum lactalbumin percentage. With a higher percentage of fat, say 3.00, the caseinogen percentage may still be kept as low as 0.21 if a 32 per cent. cream be used; and even with a 16 per cent. cream the percentage need not be higher than 0.54.

In the severer cases of chronic gastric catarrh it will usually be found by observation that a low percentage of fat gives better results than a medium or high percentage (2.50 to 4.00), and in such cases a combination of milk and whey at first may be much better borne by the stomach than a cream and whey, or a cream, milk, and whey mixture. In such a modification the fat percentage and the caseinogen percentage are nearly equal, the latter being four-fifths of the former, as is indicated by formula (17); and, as larger quantities of milk are added, this same ratio of fat to caseinogen is maintained, the percentages being kept under control by means of formulæ (23) and (24). After a time the fat may be increased more rapidly, if desired, by calculating out the quantities for any chosen percentage combination by means of the regular formulæ (1), (2), (3), (4), and (5).

Partial Predigestion. While digestive equilibrium can be secured by a sufficient reduction in the percentages of the proteids and fat, it must not be overlooked that an artificial mixture containing less than 1.50 proteids does not furnish what has been shown to be a satisfactory living ration for any but the youngest infant. It is true that life can be supported indefinitely upon a mixture containing a proteid percentage something more than 1.00, but, with this, satisfactory gain in weight and fibre cannot be expected after the first few weeks of life. A percentage of 1.50 for the proteids must, therefore, be secured just as soon as the infant's digestive powers will permit of it, and to this end partial predigestion of the mixture will give material aid. For example, an infant of four weeks who failed to digest satisfactorily a mixture containing 2.88 fat and 0.63 total proteids was enabled by partial peptonization perfectly to assimilate a mixture in which the total proteids were raised to 1.00. Such a gain in the proportion of proteids that can be assimilated fully justifies the resort to this expedient. In the more difficult cases partial predigestion of the cream and milk is often a very valuable help. Here the cream and milk, together with a portion of the diluent about equal in quantity to that of the cream and milk combined, may be partially predigested for eight, ten, twelve, or fifteen minutes at a temperature of 105° F., after which the mixture is rapidly raised to a temperature of 150° F. to check further action of the pancreatin, and then cooled before the addition of the whey. Or, the whey may be added to the warm milk and cream mixture after peptonization has been carried on for five to seven minutes, and the process then continued for five to eight minutes longer, after which rapid heating to 150°.

Preparation of the Mixtures. There is no question that the best and most accurate results are obtainable when the ingredients of the mixture are prepared and combined in the laboratory. If for various reasons this is impracticable, perfectly satisfactory results may be secured by home modification in the hands of an intelligent mother with materials supplied by the laboratory.

Even in the absence of laboratory help very satisfactory results can be obtained by applying these principles of computation to the best materials that come to hand. While there will be divergences between the actual and theoretical percentages in the resulting mixture, the same flexibility of variation will be afforded, and relative increase and decrease in the initial percentages can always be effected, according to the demands of the case. The most important prerequisite is a cream of fairly constant fat percentage. This being given, the proteid percentages may be reckoned on the theoretical basis with comparative accuracy.

For most of the modifications that will be used under these conditions two quart jars of whole milk a day will be sufficient, one to supply

the cream and the separated milk for making the whey, the other to supply the whole milk and to make up any deficiencies in the quantities of cream and whey obtained from the first bottle. Many specimens of bottled milk show a considerable rise of cream even when first delivered, and a few hours of standing in ice or ice and salt will add considerably to the separation, which can be clearly seen at the top of the bottle. By means of a glass siphon the lower separated milk may be drawn off and kept for making the whey, while the upper creamy layer will be left in the bottle to be used as the cream. Whey made from this separated milk, while not entirely free from fat, will contain only a very minute percentage of it.

The cream remaining in the bottle should be thoroughly stirred to obtain uniformity of composition, and samples of this should be taken for several days and analyzed for the fat percentage, an average of which should be taken for the fat percentage of the cream to be used in the modification. If this be impracticable it will be safe to assume for the purposes of calculation that it averages 16 per cent. After all, in any given case the actual percentage of fat in the mixture is not so important as the relative changes that may be made. If the infant can digest a certain proportion of fat, it does not matter whether it actually be 2.00 per cent. or 2.25 per cent. A relative increase or decrease of 0.25 per cent., for instance, would raise or lower either percentage by about the same amount, and effect the desired change for this particular baby. The only disadvantage in dealing with uncertainties in the actual percentages of the component milk fluids of a mixture is that the physician cannot so sharply crystallize his experience in percentage feeding as to gain an accurate estimate of the significance of definite percentages as applied to digestive capacities.

In preparing the whey the separated milk is warmed to a temperature of 100° F., and essence of pepsin, liquid rennet, or a junket tablet added to it. About two teaspoonfuls of essence of pepsin to the pint are required, while liquid rennet, according to White and Ladd, is active in the proportion of one drachm to two quarts. The junket tablet is a cheap, convenient, and very efficient means of precipitating the curd, and has been generally preferred by mothers who have tried all three agents.

The milk is kept at 100° F. until coagulation takes place, and it is then put aside in the refrigerator to favor contraction of the curd and exudation of the whey. At the end of half an hour the solid curd is to be cut into small cubes, put into a freshly-boiled cheese-cloth bag of double thickness, and allowed to drain simply by gravity, since squeezing forces some of the curd through the meshes of the bag. After the whey is thoroughly drained it should be heated to a temperature of 150° F. in order to destroy the rennin, and again cooled before being

finally mixed with the other fluids.[1] When partial predigestion of the milk and cream has been effected this heating of the whey is not necessary, unless it be desired for its Pasteurizing action. Otherwise, in combination with raw milk the excess of rennin in the whey would cause precipitation of fresh curd.

All that now remains is to mix the cream, whey, and whole milk with the diluent in which the milk sugar has been previously dissolved, divide the mixture into bottles each containing the amount for one feeding, and put away in the refrigerator.

In conclusion, it may be stated that differential modification of the proteids is not offered as a panacea for all the difficulties of infant feeding. In some cases even with the most carefully thought-out combinations disappointment must be expected. In a very few cases the addition of whey to the mixture in any proportion has seemed to produce pain and indigestion. That such infants became comfortable under the use of a 1 in 32 dilution of condensed milk probably indicates that the power of digesting proteids was very weak, since this dilution of condensed milk contains only about 0.26 per cent. of proteids, a proportion considerably below any of the total percentages tried in the differential modifications. It is evident, therefore, that in some cases whey does not seem to be well borne. These few failures, however, in a rather extensive experience up to the present time, simply serve as the exceptions that prove the general rule.

In a large number of other infants, of from four to five months or older, most of whom suffered from serious catarrhal disease, the result of previous faulty methods of feeding, whey has been perfectly borne, and has yielded results which seemed impossible under other forms of feeding. In not a few of these cases whey has formed the almost exclusive means of supplying proteids in mixtures consisting of cream and all whey. In all these cases the improvement of nutrition under whey modifications has been striking and comparable only to that to be sometimes attained by resort to the breast milk of a perfectly satisfactory wet-nurse.

After all, the last word upon infant feeding still remains to be written; but it is confidently claimed that differential modification has brought us several steps nearer to the hoped-for goal. Further study of its remarkable possibilities may yet explain and correct the few failures that occasionally occur.

[1] This temperature, 150° F., is lower than the writer has elsewhere recommended (170° F.), but according to White and Ladd's experiments, the lower temperature is sufficient to destroy the rennin and does not injure the whey by coagulating a portion of its lactalbumin, a change which begins, as Hammarsten has shown, at a temperature somewhat below 170° F.

REVIEWS.

A Medico-legal Manual. By William W. Keysor. Burkley Printing Co., Omaha, 1901.

As the scope of medical science widens and the list of accessory subjects more or less closely allied to medicine proper lengthens, the small manual becomes almost a necessity to the general practitioner who realizes that he is expected to have at least a speaking acquaintance with all the various specialties. While this applies more particularly to specialties in the commonly accepted sense of the word, and the subject of medical jurisprudence is really an integral part of general medicine, it is nevertheless true that this important study is apt to be too much neglected by the student during his academic course. Hence, he is confronted at the very outset of his professional career, before even he has left the sheltering walls of the hospital—his second alma mater—with problems which because of their purely practical or civic nature have never obtruded themselves on his too theoretical mind. When suddenly called upon to give testimony, for instance, it is a comfort to learn from a friendly legal brother just what, in the opinion of an intelligent jury, one is expected to know, and above all to have observed and remembered in any given case.

There is a constant danger of taking too one-sided a view of topics belonging chiefly to one's own particular work, forgetting that these same topics may in an equal degree interest the members of an allied profession, not to speak of the general public, who, however, approach the subject from a somewhat different direction. Mr. Keysor's book is for this reason most suggestive; it is written by a lawyer for a doctor, and while not intended for a complete text-book of *medico-legal science*, as the author prefers to call his subject, presents in a condensed form the information necessary for a physician to possess. The arrangement of subjects is excellent, the style easy and quite free from objectionable technicalities. Much information of a purely practical kind is interwoven with an able exposition of general principles and definitions which sufficiently attest the author's sincere appreciation of the philosophical and moral sides of his subject. The chapter on opinion evidence, while not altogether palatable reading for a doctor, well deserves a careful perusal. The abuses in this field have long occupied the columns of the laic press and form no inconsiderable part of the stock in trade of the professional joke-maker. The author's remarks, if true—and he seems an eminently fair-minded man—show a deplorable state of things in this respect.

While the book is intended principally for the use of those practising in Nebraska, the differences between the laws of that State and those of other States are indicated with sufficient freedom to make the book a useful addition to any doctor's library. R. M. G.

A TREATISE ON APPENDICITIS. By GEORGE RYERSON FOWLER, M.D., Professor of Surgery in the New York Polyclinic; Surgeon to the Methodist Episcopal Hospital; Surgeon-in-Chief to the Brooklyn Hospital, etc. Second edition, revised and enlarged. Pp. 235; 58 illustrations; 13 plates, 5 colored. Octavo. Cloth. Philadelphia: J. B. Lippincott Co.

THE first edition of Fowler's *Appendicitis*, consisting of a revised reprint of a series of articles which appeared in the *Annals of Surgery*, undoubtedly contributed largely to the pioneer work then being accomplished in this disease. "Much of the book has been rewritten, several chapters recast, and two new chapters added," one on the differential diagnosis, and one on the medical treatment of appendicitis. The work is well printed on excellent paper and beautifully illustrated. Unfortunately the author clothes his thoughts so liberally with words that one easily loses sight of the idea or fact presented and sees only the verbal great-coat which hides it.

Although it is fashionable to believe that almost every pathological condition is due to microbic infection we are glad to observe that Fowler maintains bacteria do not necessarily play a part in all cases of subacute and chronic relapsing appendicitis. He suggests, from a clinical and microscopical study, that, in many of these cases, vascular and nervous lesions in the mesoappendix precede and produce the changes in the appendix, and that angulation or the pressure of an overfilled colon may lead to an active or passive hyperæmia of the organ. He considers traumatism and indigestion (enteritis?) scarcely possible as etiological factors. We have had the opportunity to observe several patients who attributed their appendiceal trouble to external injury, and Small (*Medical Record*, September 10, 1898) reports thirteen cases of appendicitis with a clear history of trauma. The instances of appendicitis preceded by digestive trouble appear to us to be quite numerous.

We find in the twenty-two pages devoted to differential diagnosis the same fault already mentioned, the essential facts are obscured by "clouds of words and lakes of ink." For instance, a table detailing the differential points between appendicitis and tubo-ovarian inflammation is given, then a paragraph each on ectopic pregnancy and pelvic hæmatocele, although gynecologists assert the former to be an almost invariable cause of the latter; next a paragraph noting the possibility of the coexistence of adnexal and appendiceal inflammatory lesions; five pages later we are greeted with ruptured pyosalpinx, and, finally, after perusing five more pages, we are again presented with a paragraph on tubo-ovarian inflammation. Any disease accompanied by vomiting, abdominal pain, tenderness, and rigidity is liable to be confused with appendicitis. We feel confident that a list of these conditions with the distinguishing features following each would be infinitely less laborious and much more lucid. Perityphlitis and paratyphlitis are recognized, and the differential diagnosis given. We note the absence of pleurisy, pneumonia, dysmenorrhœa, intestinal parasites, acute chemical poisoning, cholera morbus, mesenteric thrombosis and embolism, and the abdominal type of influenza, all of which may be mistaken for appendicitis. In the table differentiating appendicitis from hepatic and renal colics we would have included jaundice and the history; in the one differentiating appendicitis and tubo-ovarian inflammation, the fact that salpingitis is usually bilateral, the pain often shoots down the thigh,

and the hymen is absent; and under gall-bladder lesions we would have included the fact that chills are commonly present.

In the treatment of peritonitis, Fowler deprecates the scouring of the intestines with gauze to remove patches of lymph, and places the patient in the elevated head and trunk posture to facilitate the passage of fluids away from the dangerous areas of absorption in the diaphragm. Theoretically, this procedure is as highly rational as ligaturing a limb in snake-bite, the poison entering the general circulation in greatly diminished quantities. It is diametrically opposed to the postural drainage of Clark, which we believe it will finally supplant.

Appendectomy is recommended as soon as the diagnosis of progressive appendicitis is assured. Concerning the time at which to operate, the author states that a case demanding operation within twenty-four hours of its onset is exceptional, but that if the patient is not practically well at the end of that time operation is demanded. Regarding the removal of the appendix in every case we gather that the author sometimes leaves it in the abdomen, contenting himself with drainage, but this is not definitely stated in the text.

To prepare a room for operation we are advised to remove everything portable except the carpet, which should be thoroughly soaked with several gallons of corrosive sublimate solution, "the carpet should be so wet that the water oozes from the latter when it is walked upon, as water is forced from a wet sponge when it is squeezed." The author might have added that the floor should have been well calked, and the surgeon should wear rubber boots.

Fowler employs the intermuscular operation when possible, practises typical excision of the appendix when conditions permit, and closes the abdominal wound when it goes directly into the peritoneal cavity, by a removable layer suture of silkworm-gut, which resembles the lacing of a shoe.

The work is concluded with a chapter on appendicular lesions from foreign bodies, typhlitis, perityphlitis, and paratyphlitic abscess.

The book is an exposition of the author's views and methods, based on an extensive personal experience. Little reference is made to the work of others. In its pages the alert surgeon will find little with which he is not already familiar; the general practitioner and occasional operator may find much valuable information whose guidance can be trusted with safety. F. T. S.

INTERNATIONAL CLINICS. A Quarterly of Clinical Lectures and Especially Prepared Articles on Medicine, Neurology, Surgery, Therapeutics, Obstetrics, Pediatrics, Pathology, Dermatology, Diseases of the Eye, Ear, Nose, and Throat, and other topics of interest to students and practitioners. Edited by HENRY W. CATTELL, A.M., M.D. Tenth series, Vols. III. and IV. Eleventh series, Vol. I. Philadelphia: J. B. Lippincott Co., 1900–1901.

WITHIN the year we reviewed the first two volumes of this series, and called attention to what we regarded as defects therein contained. To Volume III. our criticisms do not apply, for whether the "symposium on genito-urinary diseases" with which it opens, or the scholarly mono-

graph on the "scientific modification of milk" with which it closes is worthy of greater commendation, it is difficult to decide, but the fact remains that there is not an uninteresting section in the volume. And what do we find? Valentine, on "Aseptic Urethral Instrumentation," concise, practical, and thorough; "Retrogenital Chancres," by Bulkley, a most industrious collection of facts along this line; from the enormous field of the St. Louis Hospital, Fournier on the "Treatment of Soft Chancres;" Lewis, with a "new ureter cystoscope," and its use in the male; Gottheil, on various syphilitic manifestations, with illustrations so lifelike that even the patient's trousers form a realistic background; Peabody for the liver and Fisher for the nervous system in syphilitics close the symposium. Therapeutics is well to the front with several practical articles, so practical that even a carping critic hesitates to suggest that Lagrange means "tuberculosis" when he writes "tubercular." Then, in medicine, a posthumous paper by Da Costa is fruitful, not only for variety of subjects, but in hopefulness of result. Bishop gives a brief account of some diseases as he has found them in the "Colored Hospital." Very satisfactory, for it shows careful observation. The prescription on page 97 ignores the fact that *spiritus* is a noun of the fourth declension. In neurology Walters gives a succinct table of the stigmata of degeneration (p. 146), evidently based on extended observations; of especial value are his preliminary remarks. Surgery, obstetrics, and gynecology, and diseases of the eye and ear each have received attention. The article by Krause on the "Use and Care of the Microscope" should be read by every laboratory worker, for he rather than the practitioner abuses his instrument. We have read this volume in the intervals of engrossing work, and although it is by no means sketchy, as one author designates his contribution, it is not lacking in freshness of thought and in capability of sustained interest. We regard it as a distinct improvement upon its immediate predecessors, and trust that its high standard may be maintained.

R. W. W.

Volume IV. of the tenth series of this valuable publication contains a number of articles written by men prominently identified with the subjects on which they have written.

The subjects are treated under seven headings—therapeutics, genito-urinary diseases, medicine, neurology, surgery, pathology, and laboratory methods, and the work is concluded with a monograph by Dr. Cattell entitled "The Etiology and Morbid Anatomy of Various Diseases," which is, in fact, a condensed quiz compend.

A. Potain contributes an article on the indications and contraindications of digitalis in treating heart disease. Renault, Pedersen, Guyon, Ohmann-Dumesnil, and Fournier all contribute to the symposium on genito-urinary diseases; A. V. Meigs lectures on "Cases Presenting Renal, Cardiac, and Pulmonary Lesions," abstracted from his clinics at the Pennsylvania Hospital, while Deaver gives a series of abstracts from his clinics at the German Hospital of Philadelphia, including descriptions of a number of operations, the technique, preparation, and after-treatment. The two articles of most popular as well as medical interest in the volume are "Mosquitoes and the Prophylaxis of Malaria," by B. Grassi, of Rome, and "Blastomycetes as the Cause of Cancer," by Roncali, also of Rome.

Grassi states that malaria is conveyed solely by mosquitoes of a cer-

tain variety under certain conditions of temperature; that it has proved impossible to produce malaria through the agency of water, air, or other insects, or through other varieties of mosquitoes, and that the biologist should be content to look no further for other causes of the disease when the conditions of the intermediate life of the organism in the mosquito are of such a delicate nature that the mere substitution of another variety of mosquito in the link of life is sufficient to break the chain. Roncali believes that cancer is a parasitic disease, and that blastomycetes, near relations of the ordinary ferments, are probably the cause.

In the AMERICAN JOURNAL OF THE MEDICAL SCIENCES for May, 1901, H. R. Gaylord, of the New York State Laboratory, published an exhaustive article in which he claims to have discovered the cause of cancer to be a form of protozoon, and in inoculation experiments has had most remarkable results. He has succeeded in producing carcinomatous and sarcomatous growths in animals by inoculation with carcinomatous and sarcomatous material as well as with pure cultures (?) of the organism. The author, however, has not described his methods of obtaining pure cultures and the culture media used, and until these important points are made clear we cannot consider that any connection between the organisms and the disease has been proved. It is only fair to Dr. Gaylord to state that he promises in a subsequent article to give the details of the culture methods, etc., used in the experiment. The whole volume is of particular interest, and should prove valuable in keeping practitioners up to the mark in the study of medical progress.

Volume I. of the eleventh series contains articles and clinical lectures by prominent teachers and clinicians of various countries, including Italy, France, England, Scotland, and the United States, though contributions from German writers have been conspicuous by their absence in the last two issues.

The contents are grouped under eight headings, namely, therapeutics, medicine, neurology, surgery, obstetrics, and gynecology, diseases of the eye, laboratory methods, and progress of medicine.

Under therapeutics there are three contributions: "Notes on New Remedies," by A. A. Stevens; "Treatment of Chronic Gonorrhœa or Gleet," by A. Renault, and the "Treatment of Eczema," by H. Hallopeau. The articles and clinics on medicine are contributed by Delafield, Batty Shaw, Marx Biss, Campbell Williams, and S. Solis-Cohen.

In the portion of his clinic devoted to the treatment of pneumonia Cohen speaks of the treatment by saline infusions, first introduced in the Philadelphia Hospital in 1889—a method of treatment the value of which we believe has not been thoroughly appreciated as yet.

Clinics by Rodman, Roncali, Elsberg, and Holmes make up the chapter on Surgery, while Deaver, Doleris, and Kynoch lecture on obstetrics and gynecology; Edward Jackson writes on "Points in the Diagnosis of Iritis and Glaucoma;" Walmsley, on "Some Practical Methods in Photomicrography," and last, but by no means least, Blackwood gives a valuable "Review of the Progress of Medicine During the Year 1900," writing on subjects in medicine, therapeutics, serotherapy, neurology, and surgery.

The work is well prepared, the articles carefully written, and the book itself published in a very attractive form. J. N. H.

A MANUAL OF MATERIA MEDICA AND PHARMACOLOGY. By DAVID M. R. CULBRETH, Ph.G., Professor of Botany, Materia Medica, and Pharmacognosy in the Maryland College of Pharmacy; Associate Professor of Materia Medica and Pharmacognosy in the University of Maryland Medical and Dental Schools. Second edition, enlarged and thoroughly revised. Pp. xv., 885. Philadelphia and New York: Lea Brothers & Co., 1901.

THIS work treats of all drugs of organic or inorganic origin which are or have been official in the *United States Pharmacopœia*, together with those of important allied species and useful synthetics, and is embellished with four hundred and sixty-four illustrations. Some four years ago we called attention to the many excellencies of the first edition. We note with interest the improvement which experience has prompted the author to make. First, as to arrangement, we note an entire revisal of the sequence of drugs derived from the vegetable kingdom; they now are arranged commencing with the simplest plant and ending with the most complex. The animal drugs begin with those derived from the lowest grade and ascend to those of the highest development. The remaining drugs, inorganic, carbon, and synthetic compounds, are arranged on a chemical basis. This is a distinct improvement, in that it follows the natural order of evolution, excepting in order of main divisions, which would be, of course, inorganic, vegetable organic and animal organic drugs. We note, also, the endeavor of the author to popularize the metric system of measurements by giving it the preference, and in this the book will find many imitators. Further, the physiological action of remedies has been extended, and toxicology has received attention. Many observations might be quoted with approval, but this may indicate the trend of the author's mind. "Arrangement by alphabetic sequence. This is the least scientific but the most popular; in fact, it is not a true system, as no tacit relationship in any particular exists between the associated subjects, save that of initial letter in spelling, which can offer to the student the trifling advantage of texical convenience." Naturally, with predominant logical faculty the matter is arranged with a view of the student's acquisition of tone perspective and ready association of correlated facts. Of matters which might have been left for other treatises, we formerly suggested the "Microscope and its use in materia medica." "Poisons—treatment and antidotes" might also be open to the same remark were it not for the fact of the great excellence of this portion of the appendix. "Prescription writing of the physician" is somewhat refreshing in the advice that an indifferent penmanship should be improved by careful practice, "so as to make sure that you know how to write before knowing what to write." This statement, evidently suggested by experience, is respectfully submitted for the consideration of State boards of medical examiners. One matter which in our opinion is quite as important for the student of pharmacy to remember has been omitted: That when a pharmacist is called upon to furnish a copy of the prescription that it should be an exact copy, *verbatim et literatim*. This we have never found done, but the alleged copy is a strange mixture of cases and genders, or an aggregation of uncouth abbreviations. The book is better for having its index in larger type than was employed in its predecessor.

This edition shows the same painstaking accuracy, extensive reading, and satisfactory treatment of the various topics; naturally with greater stress being placed upon the vegetable materia medica, although the inorganic and synthetic compounds are by no means neglected. We are still of the opinion that the pharmaceutical, rather than the medical, student will find it better adapted to his requirements. The latter will probably devote less time to the substance and more to what it will do and for what it is used. The work has occupied the leading place which we predicted for it, and this edition makes it still more worthy of its prominent position. R. W. W.

AN AMERICAN TEXT-BOOK OF PHYSIOLOGY. Edited by WILLIAM H. HOWELL, Ph.D., M.D., Professor of Physiology in Johns Hopkins University. Two volumes, royal octavo, of nearly 600 pages each, fully illustrated. Philadelphia and London: W. B. Saunders & Co., 1900.

THE science of physiology changes so rapidly and new ideas and theories displace old and accepted ones with such swiftness that new editions of a text-book on the subject are frequently necessary in order to keep pace with the general advance. The first edition of the *American Text-book of Physiology* at the time of its publication represented the very latest phase of the subject; but in the comparatively short time since it appeared, owing to the rapid advance in this as in allied branches of medical science, as well as to the exhaustion of the first edition, the second has become necessary, and is now given to the profession, embodying the latest ideas on the subject. A critical review of the *Text-book* as a whole is hardly necessary, as it is known to the student and practitioner as a standard work by the most eminent men in this branch in the country, and the present edition is a worthy successor of the preceding one. Written by a number of men, most of them professors of physiology in the leading medical schools of America, each of whom has contributed special chapters on the subjects they are most fitted to write upon and expound, the work has an authority and a breadth that are seldom attained by a one-man book, and, though many of the papers slightly overlap each other in their scope, the whole result is remarkably harmonious. Many parts of the second edition have been rewritten, with numerous excellent illustrations, notably the chapter on the Central Nervous System, which has been much extended and brought thoroughly up to date, while the section on Physical Chemistry is a very valuable and ably written addition that will prove of great help to the student of physiology, as the subject has come into a great deal of prominence lately. In the other sections many old theories have been discarded where they have been shown to be wrong, their places being taken by the latest discoveries and the subjects treated from the newer points of view. Throughout the book references are given in numbers, forming quite a complete bibliography in most sections, though in others they are not so frequent. Owing to the rather unwieldy size of the first edition, the present one has been brought out in two volumes, each of a very convenient size, of about six hundred

pages each. There have also been some slight changes in the order of subjects, necessitated by the division of the work, though the general arrangement is the same as before. A table of contents in each volume and a revised and enlarged index are a very considerable aid in tracing out any desired subject. The whole work is excellently written and well fulfils its mission—that of a standard American text-book.

G. M. C.

PHYSIOLOGY: A MANUAL FOR STUDENTS AND PRACTITIONERS. By HOWARD D. COLLINS, M.D., Assistant to the Attending Surgeon of the Roosevelt Hospital; Assistant Demonstrator of Anatomy, College of Physicians and Surgeons (Columbia University), New York; and WILLIAM H. ROCKWELL, JR., M.D., Assistant Demonstrator of Anatomy, College of Physicians and Surgeons (Columbia University), New York; Member of Association of American Anatomists. Pp. viii., 323. Philadelphia and New York: Lea Brothers & Co.

To write a manual is by no means an easy task, for it necessitates a thorough knowledge of the subject, a fine discrimination of the relative importance of topics, and an accurate judgment of the value of recent additions to special knowledge. Finally, the language should be terse and the statements without ambiguity. When the authors have reached this degree of excellence a manual is useful in two ways: for the student who from it may acquire the essential facts as a basis upon which to rear a more elaborate structure from reading or lectures, and for the practitioner who wishes to systematically refresh his memory and know the modern phases of old questions. In both form and substance we find much upon which to congratulate the student. Inasmuch as modern therapeutics is based upon accurate physiological knowledge the busy practitioner will find satisfaction in perusing its pages. He will find explanations of well-known clinical facts and for himself draw conclusions of value. For instance, a reading of the "time of the cardiac cycle" (p. 62) gives ready suggestion of the speed of tiring of the rapidly acting heart. Or if "localization of brain function" has become a mere shadow on pp. 199 *et seq.*, he will find a forceful, if brief, presentation. Or if embryology has survived as part of a dry introduction to text books in obstetrics, pp. 266 *et seq.*, will come as decidedly simple and fairly complete view of the subject. The neuron is dismissed rather briefly (p. 165), but possibly the authors think that enough has been written from other stand-points. We have indicated briefly how this book can be useful, and in so doing have shown our appreciation of the very excellent work of the authors. The way of the student has been made easier; let us hope that he learns his lessons more thoroughly.

R. W. W.

DISEASES OF THE EAR, INCLUDING THOSE OF THE NOSE AND THROAT IN RELATION TO THE EAR. By THOMAS BARR, M.D. Third edition, revised and partially rewritten. Glasgow: James Maclehose & Sons, 1901.

THIS excellent manual for the use of students and practitioners now appears in its third edition. It is one of the most practical, and, for its size, complete books of the kind which we have. One especially attractive feature in the work is the concise and authoritative manner in which the author speaks. Every topic shows that it is discussed from the stand-point of one who is a thorough master of his subject.

The illustrations of the work are superior to most of those to be found in books of this character in the possession of particular value as illustrating the text which they accompany. Some of the photographs, such as those of the facies in adenoids or in facial paralysis, are much above the plane of those usually used for the illustration of such conditions.

The discussions of the various subjects are arranged in such a way as to make them very easy of reference, and one cannot but feel that the great success obtained by Dr. Barr's book as a text-book has been fully justified by the skill with which he has arranged his subject-matter.

F. R. P.

ATLAS OF THE NERVOUS SYSTEM, INCLUDING AN EPITOME OF THE ANATOMY, PATHOLOGY, AND TREATMENT. By CHRISTFRIED JACOB. Edited by EDWARD D. FISHER, M.D. Philadelphia and London: W. B. Saunders & Co., 1901.

THE idea dominating the writing of this book was that accurate pictures teach more than long verbal descriptions. The idea is well carried out, and the result is a very useful book. There are a few diagrams, but most of the plates represent actual sections. It will be of great use to the student wrestling with the much-dreaded question of nervous anatomy and pathology. Interest is added to many of the plates by the fact that oftentimes a short history of the case from which the specimens were obtained is given. The first twenty-two pages contain a description of the general anatomy of the nervous system. This is followed by chapters on development and physiology. Then comes general pathology, including causation, symptomatology, and methods of examination, and, finally, brief but good sketches of the lesions in special diseases. The book is most excellent, and should be bought and studied by all who are interested in nervous diseases. C. W. B.

PROGRESS

OF

MEDICAL SCIENCE.

MEDICINE.

UNDER THE CHARGE OF

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On the Treatment of Aneurisms by Injections of Gelatin.—GRENET and PIQUARD (*Arch. Gén. de Méd.*, 1901, 78, Ann., n. s.v. 641) consider carefully the question of the value of the treatment of aneurism according to the method of Lancereaux by the injection of solutions of gelatin. The study is based upon one personal observation and a careful analysis of 100 cases in literature. They divide the cases into four groups: In the first, including eleven cases, the observations are without value with regard to the result of treatment. In the second group of five cases there were grave sequels which may have been due to the treatment. In a third group of twenty-five cases the treatment had no apparent influence. In the fourth group there was more or less temporary or permanent improvement—forty-nine cases.

In a discussion of these cases, however, they come to the conclusion that the relation of these apparently good results to treatment is extremely doubtful. After inquiring into the evidence concerning the absorption and the coagulating power of gelatin injected subcutaneously, and into the dangers of such methods, they come to the following conclusions:

1. Injections of gelatin are indicated, according to Lancereaux, only in saccular aneurisms; nevertheless, according to Bourdillon, their favorable action is not limited to the encouraging of the deposition of clots, but may be exercised also even in fusiform aneurisms.

2. The pain and fever which often follow injections result from the action of the gelatin itself.

3. The possibility of embolism and of massive coagulation is not positively demonstrated.

4. It is possible, if gelatin passes into the blood without undergoing transformation, that the injections may, in certain voluminous aneurisms of

large size with feebly resistant walls, determine a deleterious increase in pressure.

5. Despite the large number of patients who have seemed to be relieved as a result of the injections it is impossible to draw positive conclusions from the statistics, inasmuch as the observations have been for the greater part insufficient, and the subjects have been rarely followed after the conclusion of treatment.

6. Experiments as well as clinical facts do not permit conclusions as to the value of treatment. It seems practically proven that gelatin injected subcutaneously is absorbed, but it is not known whether it is absorbed as gelatin. Even if one assumed that it passes into the circulation without modification it would yet be necessary, in order to learn its therapeutic action, to study not only its immediate influences, but also its later effects, which are, perhaps, as a comparison with peptone would suggest, entirely different.

7. The study of the action of gelatin in subcutaneous injections is to be reconsidered from a clinical stand-point, and is as yet incomplete experimentally.

The Experimental Production of Hepatic Lesions of Splenic Origin.—CHAUFFARD and CASTAIGNE (*Arch. de méd. exp. et d'anat. path.*, 1901, xiii., 321) have made an interesting set of experiments demonstrating the possibility of the passage of various harmful and innocuous substances from the spleen to the liver, with subsequent localization in that organ and the production, sometimes, of pathological changes limited to the liver and spleen. These observations are of interest in connection with the recent studies of Collet and Gallavardin upon primary splenic tuberculosis with secondary hepatic involvement which have recently been referred to in this JOURNAL. They appear to have proved from an experimental stand-point (1) that solid particles introduced into the parenchyma of the spleen may reach the liver and become localized there; and (2) that tuberculosis limited to the liver may follow a primary localized splenic tuberculosis. By a series of experiments they were able to demonstrate the fact that, when injected into the splenic pulp, carmine reached the liver only after several days, while, when the injection is made into the splenic artery, the substance is to be found in the liver in twenty-four hours.

Three interesting series of experiments were made with intrasplenic inoculation of tuberculosis in guinea-pigs. In the first series six animals were inoculated with a culture of human tuberculosis and all killed inside of about two months. In all instances the lesions were purely splenic. In a second series six guinea-pigs were inoculated with tuberculous products from the spleen of a subject dead of general tuberculosis of extreme virulence. In all of these instances a more or less general tuberculosis developed. In a third series six guinea-pigs received an intrasplenic injection of several drops of a triturate of the tuberculous spleen of a guinea-pig dead of experimental tuberculosis. In practically all of these cases there were found, after one month to a month and a half, caseous tuberculosis of the spleen and fresh embryonal tuberculosis of the liver. In no case were any tuberculous lesions found elsewhere. They believe that these results show that, accord-

ing to individual conditions of virulence of the bacilli, splenic tuberculosis may remain limited to this organ or extend to the liver in a strictly splenohepatic type, or, passing onward, become disseminated.

Nervous Complications and Sequelæ of Malarial Fever.—BUSQUET (*Rev. de méd.*, 1891, xxi., 441) reports the case of a patient who had four distinct attacks of malarial fever in three months, each of which was associated with interesting nervous phenomena. In November, 1897, the patient, while in Madagascar, had a pernicious comatose paroxysm. After his recovery he began to suffer from girdle pains, which, however, yielded to treatment with quinine. In January, 1898, he began again to have attacks of intermittent fever with a rapidly developing anæmia, as a result of which he was sent to Marseilles. On May 16th the patient had a chill. There was marked paresis of the right arm and leg, the right arm showing a rhythmical tremor which persisted during effort, and as a result of which he found it difficult to feed himself. The right leg when flexed showed spontaneous epileptoid tremor, with oscillations of great amplitude; general sensation good. The right patellar reflex was greatly exaggerated and accompanied by a clonus. The left was slightly exaggerated; there was ankle clonus on the right side; the plantar reflex absent on the right, increased on the left. There was incontinence of urine. The blood showed malarial parasites, both of the acute cycle and crescentic. (The observer states only that amœboid and crescentic forms were found.—W. S. T.) Under quinine the fever and all the nervous symptoms entirely disappeared. In four days most of the symptoms had yielded. In two weeks the treatment was stopped. In five days the nervous symptoms reappeared, and three days later incontinence of urine. On June 10th there was a febrile paroxysm, and on the following day incontinence of feces. Under treatment by quinine the symptoms again cleared up in a few days, though the incontinence of urine lasted for eight days. Treatment by quinine was stopped after ten days. Four days later the incontinence of urine appeared, and on the following day there was another febrile paroxysm. He was then given a hypodermic injection of 2 grammes of hydrochlorate of quinine, and afterward a gramme a day for eight days, then 0.5 up to July 12th. Three days later fever and incontinence of urine again developed, which yielded once more in a few days to quinine. On July 26th the patient left the hospital feeling well. The authors believe that the nervous phenomena were probably due to the direct irritation of the central nervous system by the parasites in the circulation.

Polymyositis.—LEPINE (*Rev. de méd.*, Paris, 1901, xxi., 426) adds an interesting case to the few instances in literature. The patient was a man, aged fifty-nine years, who entered his clinic on January 24, 1901. He was a cabinetmaker, of good family and personal history, and excellent habits. Eight months before entry he began to suffer from intermittent pains in the head, of moderate intensity, with occasional lancinating pains in the left side, in the mammillary region.

Three months before entry the patient discovered a swelling in the right temporal region, a small, œdematous, slightly tender, but rather hard tumor.

This lasted three or four days, during which there was considerable difficulty in chewing. After several days this disappeared, and a similar swelling appeared on the right, extending, however, to the eyelids so as to cause complete closure. After fifteen days these symptoms disappeared. At this time extremely severe pains appeared in the lumbar region, especially on movements of flexion and rotation. Six days before entry there appeared on the dorsal surface of his right forearm a small œdematous swelling, which was associated with sensations of pricking. From this the œdema spread over the entire forearm and dorsal surface of the hand. The patient was thin and pale. The forearm showed a glistening œdema, somewhat reddened, owing perhaps to applications of tincture of iodine, hard, but neither hot nor tender. A softer œdema was present on the back of the hand. Nothing was to be made out on physical examination of the back. The spleen was enlarged, and there was an anæmia of two million red blood-corpuscles; the colorless corpuscles were apparently normal; the hæmoglobin relatively diminished. Cultures from the blood were negative. The urine was free from albumin. The patient was treated by aspirine. The lumbar pains disappeared, while the swelling of the forearm progressively diminished in the course of several days.

The author discusses the term dermatomyositis. He prefers the term polymyositis to dermatomyositis, inasmuch as the cutaneous eruption observed in some cases is not a necessary symptom. He does not consider Lorentz justified in separating dermatomyositis from polymyositis hemorrhagica.

The Clinical Diagnosis of Infarctions of the Kidney.—R. SCHMIDT (*Wiener klin. Wochenschrift*, 1901, xiv., 451 and 486), after calling attention to the fact that most observers have held that the diagnosis of infarction of the kidney is rarely possible, reviews seven cases, five out of the literature and two from the clinic of Prof. Neusser, in Vienna, in which the symptoms were carefully observed during life, necropsy proving the nature of the lesion. After considering the various symptoms he comes to the following conclusions with regard to differential diagnosis:

1. In every case of renal colic it would appear to be advisable first to settle the question as to whether it is of intrarenal (increased pressure, necrosis) or of extrarenal—that is, ureteral (passageverlegung).

2. Renal pain of intrarenal origin remains in general more localized in the actual renal region; the kidney, especially in infarction, is exquisitely tender on pressure, the pain is more continual; it is sometimes accompanied by very intense albuminuria of sudden onset or with a sediment similar to that in nephritis.

3. Colic pain of extrarenal—that is, ureteral—origin has a greater tendency to radiate in the course of the ureters; there is tenderness of the ureters on pressure; this may result in an acute hydronephrosis; the pain is more intermittent.

4. Renal colics of intrarenal origin may be caused by:

(*a*) Torsion of the vascular pedicle in wandering kidney.

(*b*) Sudden congestion in richly vascular malignant tumors.

(*c*) Chronic nephritis with an acute inflammatory exacerbation.

(*d*) Renal infarct.

5. With regard to differentiation within these groups one should consider that pain on pressure over the kidneys is greater and more commonly present in renal infarct than in chronic nephritis.

High pulse tension speaks against infarct.

Onset of the attack of colic during rest in bed is common in infarct. A relation between the attack of colic and mechanical insults often occurs in cases of torsion of the vascular pedicle and in acute exacerbations of chronic nephritis.

An apoplectic onset of the pain at full intensity is especially common in infarct.

Marked hæmaturia is common in the acute exacerbations of chronic nephritis, but rare in infarct.

Intense albuminuria of sudden onset and rapid disappearance, without abnormal sediment, occurs in infarct.

6. Enteroptosis is an unfavorable complication from a prognostic standpoint in renal infarct; it favors the onset of reflex vomiting.

7. Decubitus on the healthy side or in bilateral lesions on the less diseased side causes an increase of pain in painful renal infarction.

8. In total closure of the renal artery there may be no abnormal appearances in the urine (complete shutting off of the kidney).

9. Oliguria or even anuria occurs, especially in bilateral renal infarcts; vesical tenesmus is not present.

On the Albuminoid Metabolism in Pernicious Anæmia and Bothriocephalus Anæmia.—ROSENQVIST (*Berl. klin. Wochenschrift*, 1901, xxxviii., 666) states that after the investigations of Bauer it was generally believed that in all anæmias there was an increased disintegration of albumin, but von Noorden and Lipman-Wulff showed that anæmia as such was not necessarily associated with pathological increase in the albuminoid metabolism; that if such occurred in an anæmic patient it spoke for the existence of other deleterious influences. In pernicious anæmia, however, Strümpell, Quincke, and Eichhorst have shown that an increased disintegration of albumin may occur, though most of the observations have scarcely been made with the exactness attained by modern methods. For this reason the author has studied eighteen cases of bothriocephalus anæmia and three of cryptogenetic pernicious anæmia in the clinic of Runeberg, in Helsingfors. In eleven out of fifteen cases of bothriocephalus anæmia, before the institution of anthelmintic treatment, there was a well-marked increase in the albuminoid metabolism. This was present not only in the cases with fever, but also in those without. Immediately after treatment and the disappearance of the worm the picture changed entirely, and there was, on the other hand, a well-marked nitrogenous retention. This was observed in all cases, even in those in which the diet and general conditions after the disappearance of the worm were not the best. In some cases there may be a retention of nitrogen even during the presence of the worm. The fact, however, that in all cases after the disappearance of the worm there was a well-marked increase in the albuminoid retention justifies the conclusion that in every case of bothriocephalus anæmia there are periods of pathologically increased albuminoid disintegration. This albuminoid disintegration is far too extensive to be dependent

entirely upon the destruction of red blood-corpuscles; it must be associated with changes in the other nitrogenous tissues of the body. The deleterious substance which produces these changes the author believes to be a poison produced by the parasite. As a general rule, the changes in the albuminoid metabolism go hand-in-hand with fluctuations in number of red blood-corpuscles, but exceptions to this rule occur. In seven cases in which the number of erythrocytes before the treatment was essentially constant there was a well-marked elevation in the albuminoid disintegration. We are thus, he believes, not justified in concluding, from a pause in the progress of the anæmia, that the poison is no longer active. In a certain number of cases the change for the better after treatment does not occur until some days after the expulsion of the worm. In five instances six to eleven days elapsed before essential change was to be noticed. This he believes to be due to the fact that the poison has not yet been eliminated. As a general rule, in these instances the elevation of temperature which commonly disappeared after expulsion of the worm remains present until the evidence of the presence of the poison, the increased albuminoid disintegration, and the anæmia begin to change for the better. In bothriocephalus anæmia the elevation of temperature stands apparently in direct relation with the poison produced by the worm; it may be regarded as a fever of absorption. In a certain number of cases Rosenqvist has found that, after expulsion of the worm, during the period in which the most marked increase in the number of blood-corpuscles begins, at a time of almost total nitrogenous retention, the quantities of phosphorus purin increased, and might even reach three times the previous figures despite the fact that the patient was on a purin-free diet. Whether this has anything to do with the increased destruction of nuclei of the erythrocytes is a question which cannot yet be decided.

In cryptogenetic pernicious anæmia the observations were essentially similar to those in bothriocephalus anæmia. Periods of marked increase of albuminoid disintegration alternated sometimes with those of distinct nitrogenous retention. These conditions varied from day to day; here, also, there was a certain parallelism between the changes in the nitrogen metabolism and those in the condition of the blood; also the elevations of temperature occurred only during the periods of pathological albuminoid disintegration.

He concludes "that bothriocephalus anæmia is a toxic anæmia. In every case of this blood disease there is, at certain periods, an increased albumin disintegration which is brought about by a poison produced by the tapeworm. This increased albuminoid metabolism is, however, not always to be made out in a given case, for despite the presence of the tapeworm there may be periods of well-marked nitrogenous retention.

"A comparison between the results found in bothriocephalus anæmia and those in pernicious anæmia from other cause shows that there is no essential difference between the albuminoid metabolism in the two diseases.

"My investigations, therefore, are strongly in support of the theory that cryptogenetic pernicious anæmia is also a toxic anæmia."

Puncture of the Sacral Canal by the Epidural Method.—CATHELIN (*La Presse Médicale*, June 15, 1901, p. 281) describes a new line of treatment for the relief of the intense pain of various diseases by the injection of cocaine

into the sacral canal. The technique is described as being extremely simple. Looking at the skeleton it will be seen that the vertebral canal ceases near the lower extremity of the sacrum. Its lower end is covered in by the sacro-coccygeal ligament. The spinous processes of the fourth and fifth sacral vertebræ are absent, so that there is normally a triangular space with the apex upward in this situation, bounded on each side by the fourth and fifth sacral tubercles, which represent the rudimentary articular surfaces. It is at the apex of this triangle that the cocaine injections are made.

For the injection an ordinary syringe of about 10 c.c. capacity is used. The needle should be six centimetres long, with a diameter of seven-tenths of a millimetre, and a bevelling of three millimetres at the point.

The patient is placed either in the knee-elbow position or on the side. After thorough disinfection of the sacral region, and with the usual precautions, the finger is pressed down the median line of the sacrum until it falls into the triangular depression described above. The needle is introduced about at the apex of this triangle and exactly in the median line. It is passed in obliquely upward and forward, and if inserted properly it will be felt to pass through the sacro-coccygeal ligament, by which it is firmly gripped.

The quantity of cocaine to be injected is four centigrammes. For the purpose a solution of the strength of 1 to 100, or, better, 1 to 200, should be used. The cocaine, it is to be remembered, does not enter the subdural or subarachnoid spaces, but is injected into the epidural space. It is not supposed to exert its effect by direct action on the nerve roots, but is absorbed by osmosis by the rich plexus of veins in the vertebral canal, and appears to act by dulling the general nervous sensibility.

This treatment is recommended for the relief of the following painful conditions: painful neuralgias of the lower extremities, sciatica, lumbago, the lightning pains of tabes, intercostal neuralgia, and gastric crises. It is further recommended for the pain in inoperable carcinoma of the rectum, for fissure in ano, for painful labor, and for painful affections of the joints of the lower extremities.

On Scleroderma.—NEUMANN (*Deutsch. Arch. f. klin. Med.*, 1901, lxx., 168) describes five carefully studied cases of scleroderma. In two of these there was a goitre; in four the condition was ushered in by rheumatoid pains, in three the diagnosis of chronic rheumatism having been made at the onset. In four there was marked pigmentation; in several so much so that the appearance of the patient was almost that of a subject of Addison's disease; the pigmentation, however, was never present on the conjunctiva or mucous membrane. In one instance, two years before death, the sclerodactylia became so marked that actual mutilation of the phalanges resulted. About the joint of the last phalanx, without any sign of local irritation, there developed, quite as in ainhum, a contraction of the white skin, which resulted in a dry necrosis of the nail and the tip of the finger as well as of the spongy end of the last phalanx. The course of this necrosis lasted several months, and was associated with severe pain. The end of the phalanx was black, dry, and mummified, and ended in a slowly developing scar formation. Out of the base of the scar protruded the very tender end of the bone.

In discussing the observations the author calls attention to the striking

likeness between the extensive scleroderma and Addison's disease. In scleroderma, however, the pigmentation of the conjunctiva and mucous membrane of the mouth is absent, while in Addison's disease the doughy swelling and thickening of the skin, with associated pigmentation in various places and absolute loss of pigment elsewhere, are never present. Moreover, the loss of strength in true Addison's disease and the more rapid course are characteristic of most, if not all, the cases.

Neumann is inclined to believe that the condition represents a chronic intoxication, probably of a non-bacterial nature.

The prognosis he considers extremely grave. Although improvements and recoveries are occasionally spoken of, the possibility of the latter he considers very slight, most cases in which recovery is supposed to have occurred having been imperfectly reported.

With regard to treatment, Neumann has obtained little result from internal medication. On the other hand, in his three last cases marked improvement has followed the persistent use of hot-air treatment.

On Occult Hemorrhages into the Stomach.—Boas (*Deutsch. med. Wochenschrift*, 1901, xxvii., 315) mentions the fact that if gastric hemorrhages are of very slight extent they may be entirely overlooked, especially in an acid medium, and he has been struck by the fact that, with careful methods, blood may not infrequently be demonstrated in specimens of gastric juice in which, macroscopically, it might never have been suspected. He prefers Weber's modification of the guaiac test, and states that special care should be taken that the tincture should always be freshly prepared. This he believes to be the most delicate method, especially if the ethereal solution, after the addition of tincture of guaiac and oil of turpentine, is shaken out in water and chloroform, and the mixture allowed to stand for a considerable time. The gastric juice to be examined should be taken by means of the stomach-tube and with great care. The vomitus often contains blood from other regions. The observations of Boas have been limited to eighty-three cases, including a variety of different conditions. He divides his results into three classes: 1. Those in which hemorrhages were constantly absent. 2. Those in which they occasionally occurred. 3. Those in which they were always found. The first group included all the cases of neuroses as well as those of gastritis anacida, with one exception, and, further, a case of subacidity, and all cases of superacidity, supersecretion, and benignant dilatation. To the second class belong the cases of ulcer of the stomach or secondary pyloric stenosis following ulcer. Blood was occasionally found also in a case of duodenal stenosis, and also in a case of syphilis of the stomach, as well as in an instance of carcinomatous stenosis of the large intestine. In the third group fell one case of hypertrophic stenosis, and all the cases of carcinoma of the stomach. In every one of these latter blood was invariably found, although in the majority it was not to be made out on gross examination.

The clinical importance of this seems to be that blood is especially likely to be present under three conditions—in typical ulcer, in tumors with a tendency to ulceration, and, finally, in conditions of well-marked chronic passive congestion. In combinations of these conditions the tendency is, of course,

correspondingly greater. It is, of course, evident that the determination of small quantities of blood in the stomach does not give us a diagnostic sign, but Boas believes it is an important addition to our methods of diagnosis. It may help us to distinguish doubtful cases of ulcer from gastric neuroses, and if it be a question of carcinoma the great frequency of the presence of blood in this condition is in sharp contrast to the fact that in chronic anacid gastritis, as well as in gastric neuroses, no blood has been found. Inasmuch, however, as ulceration which occurs in the majority of all cases of carcinoma is not a very early symptom, the presence of blood in most instances will hardly help us to an early diagnosis. Boas further raises the question as to whether the constant loss of small quantities of blood may not play an important part in the development of the so-called carcinoma cachexia.

SURGERY.

UNDER THE CHARGE OF

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The Advantages and Disadvantages of Drainage after Abdominal Operations.—ROBB (*Journal of the American Medical Association*, July 6, 1901) reports two series of cases, in the first of which there were 114 and in the second 108 consecutive unselected abdominal sections without a death. In a paper published in 1890 the author summarizes the indications for drainage as follows: 1. To provide a means of escape for the serous oozing which follows the separation of broad adherent surfaces. 2. To guard against septic peritonitis from retained pus from the tube, ovary, or other viscus. 3. To remove fluid in cases of persistent capillary hemorrhage. 4. To provide against hemorrhage in cases of hysterectomy when the pedicle is dropped. 5. To drain the peritoneal cavity and starve out the disease in cases of chronic or tubercular peritonitis. The following objections to the insertion of drainage-tubes have been formulated by Welch: "1. They tend to remove bacteria which may have gotten into a wound from the bactericidal influence of the tissues and animal juices. 2. Bacteria may travel by continuous growth or in other ways down the sides of the drainage-tubes, and so penetrate into a wound which they otherwise would not enter. We have repeatedly been able to demonstrate this mode of entrance into a wound of the white staphylococcus found so commonly in the epidermis. The danger of leaving any part of the drainage-tube exposed to the air is too evi-

dent to require mention. 3. The changing of dressings necessitated by the presence of drainage-tubes increases in proportion to its frequency the chances of accidental infection. 4. The drainage-tube keeps asunder tissues which might otherwise immediately unite. 5. Its presence as a foreign body is an irritant and increases exudation. 6. The withdrawal of tubes left for any considerable time in wounds breaks up forming granulations—a circumstance which both prolongs the process of repair and opens the way for infection. Granulation tissue is an obstacle to the invasion of pathogenic bacteria from the surface, as has been proved by experiment. 7. After the removal of the tube there is left a track prone to suppurate and often slow in healing." To these Halsted has added: 8. "Tissues which have been exposed to the drainage-tube are suffering from an insult which more or less impairs their vitality and hence their ability to destroy or inhibit organisms."

But beside increasing the chances of infection, drainage not infrequently gives rise to various post-operative complications. Of these Clark mentions: 1. Obstruction of the bowel. 2. Fecal fistulæ. 3. Vesical complications. 4. Post-operative herniæ. It is a well-known fact, and one proved by the most conclusive experiments, that under normal conditions the peritoneum can dispose of pyogenic organisms in no inconsiderable quantities without the occurrence of peritonitis. Nor must it be forgotten that drainage does not by any means always remove all foreign fluids and infectious matter, so that in not a few cases its employment will offer all the many disadvantages referred to above without accomplishing the main object. Clark has noted that the introduction of drainage material handicaps the peritoneum in three ways: 1. The normal peritoneal currents are disturbed, consequently the circulation of fluids and foreign matter toward the diaphragm is retarded. 2. A reactive inflammation is set up about the drain, limiting and impeding the action of the peritoneum. 3. Within a few hours the general peritoneum is cut off from all participation in the work of absorption by the wall of adhesions around the drain. In place of the natural agencies the work is thrown upon an agent which at best can only remove the fluid from a small pocket.

When gauze is used it soon becomes choked by the serous or bloody fluid which fills up its meshes and quickly coagulates. A limited quantity of fluid will be removed during the first two hours, but after that the drain acts like a plug, by preventing the outflow of fluid, which then accumulates in the dependent pockets.

The methods for prevention or the removal of infective material without the employment of drainage may be summarized as follows: 1. A thoroughly aseptic technique. 2. The controlling of all hemorrhage and oozing as far as possible. 3. Careful manipulation, so that all unnecessary bruising of the tissues is avoided. 4. A perfect toilet of the peritoneal cavity. 5. The removal as far as possible of infectious foci. 6. The use of irrigations with salt solution. 7. If necessary the reopening and thorough cleansing of the cavity. 8. Proper after-care of the patient. The author states that he has used drainage only once in 222 consecutive cases, and in this case the only reason that it was used was that there was a large pus sac present, communicating with the vagina and peritoneal cavity, which it was impossible

to remove. In the author's two series of 222 cases, he reports finding pus in 65, or 28 per cent. After a wide experience before 1893, with drainage, and practically not having used it since then, the author believes that patients, as a rule, do very much better if drainage is not used. Not only have the immediate results been better, but the ultimate results, such as the occurrence of hernia and intestinal adhesions, have been avoided.

The Treatment of Abdominal Aortic Aneurism by a Preliminary Exploratory Cœliotomy and Peritoneal Exclusion of the Sac, followed at a Later Sitting by Wiring and Electrolysis.—MATAS (*American Medicine*, June 29, 1901) states that of the fifteen reported cases treated by this method all but three have died. A careful examination of the histories of these three cured cases tends to bear out the conclusion that aneurisms which originated low down on the abdominal aortic tract, especially below the superior mesenteric, all other conditions being equal, are much more favorable for attack by this method than those seated higher up in the cœliac area. The objections to this method of treatment are: 1. The cure of the aneurism may lead to the death of the patient by obliterating the orifice of important visceral arteries. This is most likely to occur in dealing with aneurisms of the upper or cœliac division of the abdominal aortic tract—*i. e.*, in about 50 per cent. of the cases. 2. Secondary rupture of the sac from the strain put upon weak portions of the sac in multilocular aneurisms after partial coagulation of the contents has taken place is particularly likely to occur in subjects of general endarteritis with atheroma. 3. Escape of wire through a large aneurismal orifice into the lumen of the aorta, with migration upward into the heart, leading to perforation, traumatic endarteritis, endocarditis, with the formation of secondary thrombi and emboli. 4. Danger of perforating the sac by stiff wire or by overcrowding the sac with too much wire. 5. Danger of extension of clot from the coagulum in the aneurism to the main artery, leading to fatal blockade at the bifurcation, with gangrene of the lower extremities. 6. Danger of rupture of sac from sudden withdrawal of abdominal support and displacement of adherent organs in the course of the exploratory laparotomy. 7. Danger of mistaking a fusiform for a sacciform aneurism. 8. Danger from emboli and thrombi following incomplete coagulation of the blood in the sac (a very rare and practically unknown occurrence in abdominal cases). 9. Danger of shock. 10. Danger of sepsis. In the presence of this formidable array of dangers which beset the application of this method, one must ask what are the conditions, if any, which are favorable to its successful application? Theoretically possible, but clinically rare, are the following conditions: (1) The aneurism should be saccular; (2) it should be unilocular; (3) it should be provided with fairly strong, resisting walls; (4) the patient should be young or middle-aged, fairly healthy, and free from general endarteritis and atheroma; (5) the aneurismal orifice communicating the sac with the lumen of the parent artery should be small; (6) the aneurismal sac should spring from the lower, inframesenteric division of the artery, preferably between the origin of the superior mesenteric and the bifurcation; (7) if given off from the cœliac region the orifice should be situated on the posterior or lateral wall of the aorta. With these ideal conditions, and with a perfect

technique, the chances of permanent cure would be immensely increased and the operation could be undertaken with great probability, almost certainty, of success. But as the most important of these conditions can never be ascertained *intra vitam*, and one is thus unable to differentiate clinically between the favorable and the unfavorable cases, the author is forced to conclude that the Moore-Corradi method as at present applied, and in spite of the undoubted improvements that have been made in its technique, is a most dangerous procedure, essentially lacking in the elements of that scientific precision and knowledge of avoidable perils which are necessary to elevate it out of the plane of empiricism and surgical experimentation. Its chief recommendation now rests upon the naked fact that in three out of fifteen recorded cases (20 per cent.), it has actually arrested the progress of aneurisms and saved life. Apart from this clinical fact, it can claim but little else in its favor except that in the presence of almost certain death from the disease when allowed to follow its natural evolution, even a remote possibility of survival by operation is better than no chance at all.

The author states in conclusion that in the light of present experience we should restrict our recommendation of the combined method to that small group of comparatively favorable cases in which the aneurisms are confined to the inframesenteric portion of the aorta, and then only after other safer methods of treatment had been tried and failed. In aneurisms situated in the upper part of the aortic tract, the boundaries of which cannot be even approximately determined, the author regards this procedure in the light of a pure experiment—a veritable surgical adventure—which would be justified solely by the imminent danger of death from rapid progress of the disease which threatened rupture of the sac, and associated with great suffering. Even then the operation could not be recommended, but should be undertaken solely at the urgent solicitation of the patient after a thorough understanding that the chances would be no less than 70 per cent. against his recovery from the operation.

A Report of Twenty four Operations Performed during Spinal Analgesia.—BAINBRIDGE (*Medical News*, May 4, 1901), after reporting in detail the results of twenty-four cases, states that the following conclusions are made from fifty cases, which include those just noted: 1. Cocaine is far more satisfactory than eucaine. The latter is less potent, more evanescent, the areas of analgesia are frequently "patchy," having the pain sense retained all around them and not being so complete below definite levels. The cocaine produces no more unpleasant after-effects than eucaine, and is decidedly more reliable. 2. Analgesia to the level of the diaphragm can be depended upon in all cases where a moderate dose of a potent solution of cocaine has been introduced by lumbar puncture. In some the analgesia is sufficient for operation on the upper extremities. 3. Complete analgesia, including the eyes, mouth, and throat, has occurred. It does not entail more severe after-effects than when the lower extremities only are involved. 4. The preparation of the patient as for a general anæsthetic diminishes all the unpleasant effects of cocaine and eucaine, and often prevents them altogether. 5. By moderate doses of bromides before the injection the initial vomiting is frequently avoided and the liability of headache lessened.

6. In neurotic patients there are often hysterical symptoms directly following the completion of the injection; but, as a rule, in a few moments a calm follows and the patient lies perfectly still. 7. Initial nausea and vomiting often occur soon after the puncture, but last only for a moment or two, and usually do not recur during the operation. As consciousness, as well as the muscular power, is preserved, the danger of the introduction of the vomitus into the lungs is practically *nil*. 8. Analgesia lasts from thirty minutes to four hours. 9. Depression after the puncture is considerable. The use of ethyl chloride (Bengue) largely prevents pain when the needle is introduced. 10. The preparation of the patient, the use of nitroglycerin by hypodermic injection, or the employment of coal-tar products with caffeine, control the headache, which is in many instances an after-effect of spinal puncture. 11. In a few cases there may be motor paraplegia or vertigo. Both are temporary. 12. Spinal puncture has not affected normal or diseased kidneys. 13. Usually the tactile power, muscular sense, and the ability to detect heat and cold are retained. The cautery at a dull red heat causes no pain, while hot water produces marked discomfort. 14. Usually the patient sleeps the first night. 15. There is often a temperature of a few degrees within eight or ten hours of the operation. Whether this is the direct result of the puncture or the effect of psychic disturbances is not determined. The circulation and respiration are not seriously embarrassed.

The Diagnosis and Surgical Treatment of Renal Tuberculosis.—Brown (*Boston Medical and Surgical Journal*, May 30, 1901) states that for obvious reasons, in this malady, no one can speak authoritatively, either as to the final results of supposed radical surgical treatment, or, on the other hand, as to the certain progress toward a fatal termination of all cases which are not treated in some way. Despite the immense amount accomplished by earnest labor in the field of tuberculosis, one must hope that something more specifically curative than the knife, sanitation, or the piney woods may soon be discovered. In other localizations of the disease the importance of early diagnosis has long been appreciated; but when the kidney is involved, recognition of the fact is apt to be unfortunately tardy. In all cases of pyelitis, nephritis, and cystitis the etiology should be determined or at least most diligently sought for. In order to secure more satisfactory results from surgical treatment, renal tuberculosis must be detected in anticipation of rather than long after the objective symptoms have become so conspicuous as not alone to render differentiation of the urine difficult, but to have involved so much of other parts of the urinary tract as to preclude a radical operation. Urinary analysis in general should mean as careful a routine search for tubercle bacilli as is customarily given to the other formed elements of a sediment. There are cases of renal tuberculosis where the lesions are not in open communication with the urinary channels, hence the microorganism is not possibly attainable for microscopical or inoculation evidence. It is not so very unusual for an open tuberculosis renal lesion to shed so few bacilli that persistent microscopical search fails to find them. Here animal inoculation should always be early resorted to. Sometimes the subjective symptoms are quite pronounced, even in the early stages of the disease; in other cases the pains are little noticed in advanced stages of the

trouble, except by the behavior of the bladder, and too often these vesical symptoms are cited as evidence that this viscus is the original and only seat of the trouble. A dull aching in the lumbar region is significant; equally so is a much more acute kind of pain referable to the kidney or ureter. When these occur as crises, associated with nausea and vomiting, renal calculus or gravel colic is most apt to be thought of. So many cases give a history of having had systemic manifestations resembling mild malaria, that they seem as not infrequent precursors to the more distinctly localized later symptoms. Often the first symptom is increased frequency of urination, but in the majority of cases this does not appear until the lower segment of the ureter has either acquired a genuine tuberculous lesion or at any rate marked hyperæmia and œdema have developed, with irritation around the mouth of the ureter. The principal objective symptoms are a kidney which is larger and more tender than normal, as well as all grades of pyuria and hæmaturia, beside a just appreciable or a very marked diurnal variation in temperature; loss of color and weight; a reaction to tuberculin; finally, the presence of tubercle bacilli in the urine derived directly from one or both kidneys. The author believes that the injection of tuberculin is valuable as an aid to diagnosis in doubtful cases. The mortality of nephrectomy for tuberculosis is low, averaging from 5 to 7 per cent. The incision varies, but the operation should be performed by the extraperitoneal route.

During a nephrectomy for renal tuberculosis, if the disease is seen to extend down the ureter to a point below the first sacral vertebra, the author does not urge that a total extirpation should then, or even at a later operation, be done. Several of his observations tend to the inference that a considerable amount of tuberculous ureter can be left with comparative safety; because, now being in a functionless state of repose, this particular focus is amenable to curative systemic processes. At the same time sufficient experience has not been accumulated to assert that a routine practice based on this presumption is always the best surgery. If total removal did not necessitate such an increased operative exposure, the radical step would better satisfy the surgical indications here just as well as in dealing with any tuberculosis. If it were thoroughly ascertained that a ureter was diseased from kidney to bladder, and the operator felt inclined to do a total extirpation or none, it might improve the patient's chances to have a primary ureterectomy of the lower half, while the proximal end of the tube was given a temporary cutaneous implantation, there to drain the kidney until an early favorable time for nephrectomy. In this order the services of both kidneys would be available for convalescence from one operation. Even in cases presenting tuberculous vesical lesions where only one kidney is similarly diseased, the author thinks that nephrectomy is indicated in a certain number of such individuals as offering the best chances for extension of life and comfort. Every reasonable effort should be made to determine the condition of each kidney before any operation is done for the relief of vesical symptoms, because nothing can be gained by this latter step so long as tuberculous débris is coming into it from above. The author states in conclusion that too great pains cannot be taken by physician and surgeon to determine the location and extent of the disease before determining upon the treatment. The integrity of the other kidney, of course, has great bearing on the surgical

aspects of any case. To determine in any particular case just what rate of progress the disease may pursue if left untreated, or what degree of immunity from some of the annoying symptoms we can promise the patient by nephrectomy, is not easy. In ward hospital cases the immediate operation appears to be the only alternative. For those who can afford climatic changes and rest a careful preliminary observation of the existing conditions of the urinary tracts should precede their travels, and the same examination, when at all indicated, should be repeated in order to keep posted regarding such an advance of the disease as to call for operation.

Orchitis and Epididymitis in Typhoid Fever.—KINNICUTT (*New York Medical Record*, May 25, 1901) reports two cases of this rare sequel or complication of typhoid fever. Eshner, in 1898, after a careful review of the literature, was able to collect only 44 cases, and Do collected the statistics of complications occurring in 14,738 cases of typhoid fever without finding a single case of orchitis and epididymitis. In Osler's series of 829 cases of typhoid fever, orchitis or epididymitis was observed only in 2 instances, both unattended with suppuration, and in the 889 cases treated by the author and his colleagues in the Presbyterian Hospital the lesion was noted only in the two cases which the author reports. It is probable that the frequency of this complication is greater than the statistics indicate. Aside from cases which presumab'y have not been reported, the fact that in the 44 cases collected by Eshner, 5 occurred after the second week of convalescence—one of these, as late as the ninth week—suggests the presumption that cases occur in which the true origin of the orchitis is not suspected. The first case, aged twenty-four years, was admitted to the hospital on the seventh day of his illness. The infection was of a moderately mild type, the maximum temperature not exceeding 104.5° F. He was treated by the cold bath, and the illness was in every way uneventful. The morning and evening temperatures were normal on the twenty-third day. There was a marked increase in the leucocytes on the fifteenth day, which lasted for three days, and then gradually disappeared. The urine was slightly albuminous, but at no time were casts found. The catheter was not used, and there was at no time any urethral discharge. There was no history nor evidence of gonorrhœal infection in the past. On the fifth day of normal temperature the patient complained of pain in the right groin and the temperature rose to 101°. Examination the next day showed that the cord was enlarged, hard, and sensitive in the inguinal canal. The following day the swelling had reached the external ring, and in the course of the succeeding twenty-four hours the morbid process had extended to the epididymis and testicle. These became markedly swollen and very sensitive. There was no effusion into the tunica vaginalis. Almost simultaneous with the swelling of the cord, phlebitis of the long saphenous vein developed. The swelling of the cord and testicle gradually subsided, and on the sixteenth day after the first appearance of the symptoms the only evidence consisted of a trifling induration and sensitiveness of the epididymis, sensitiveness along the course of the saphenous vein, and moderate swelling of the leg and thigh. When examined ten weeks later all physical signs of a lesion of cord, epididymis, and testicle were absent. The second case was thirty-four years of age, and developed

orchitis and epididymitis at the end of the febrile period. Examination showed the seminal vesicles to be normal, the prostate enlarged but not tender, and some fluctuation over the testicle. Aspiration at the point of fluctuation was made, and a small quantity of pus obtained; this contained the typhoid bacillus in pure culture. The swelling and sensitiveness of the cord, testicle, and epididymis have only partially subsided, and there is still a sinus leading to the body of the testicle through which minute shreds of necrotic tissue are occasionally extruded.

In the fifty-three cases of testicular inflammation occurring in the course or during the convalescence of typhoid fever, which comprise the literature of the subject, suppuration developed in thirteen. Bacteriological examination demonstrated the presence of Eberth's bacillus in pure culture in the pus from six of the cases. In a single instance pyogenic cocci alone were found. The remaining six cases were reported prior to or about the date of Eberth's discovery of the specific bacillus of typhoid fever.

In one non-suppurative case Eberth's bacillus was found in pure culture in the sero-sanguinolent fluid obtained from an aseptic puncture of the testicle.

In view of the bacteriological findings, the usual origin of orchitic lesions in typhoid fever cannot be doubted. Apparently only exceptionally is the infection due to other micro-organisms than Eberth's bacillus. It remains to consider the probable channels of infection.

It is probable that the bacilli reach the testicle both by the blood stream and from the urethra through the intermediary of the vas deferens. That Eberth's bacillus in great numbers is found in the urine in a large percentage of cases of typhoid fever is now well known.

It may be of interest to analyze briefly Eshner's forty-four cases and the nine additional ones which the author is able to add, of orchitis and epididymitis occurring in the course or during the convalescence of typhoid fever, comprising all cases found in the literature of the subject which give sufficient detail to be of value.

Sixteen cases developed during the course of the fever. Of these, one occurred during the second week, six during the third week, two during the fourth week, one during the fifth week, one during the sixth week, two during the seventh week, two "at defervescence," and one at a time not definitely stated. Thirty-five cases developed during convalescence. Of these, eleven developed during the first week, seven during the second week, three during the third week, one during the fourth week, one during the fifth week, one during the sixth week, eleven at a time not definitely stated. In two cases the date of development is not given. In two cases the inflammation affected both sides, in forty-five it was unilateral, and in six cases no statement is made of its localization. Of the unilateral cases, twenty-two were on the right side, twenty-one on the left, and in the remaining two it is not stated on which side. The epididymis only was involved in seven cases; the testicle only in sixteen cases; both epididymis and testicle in twenty-six cases; and in the remaining four a distinction is not made between the testis proper and the epididymis. There was effusion into the tunica vaginalis in nine cases; in ten, it is noted that such effusion was absent; and in thirty-four no statement is made on this point.

Suppuration occurred in thirteen cases, partial necrosis in five cases, complete necrosis in two cases, and death in two cases, but without apparent relation to the complication. Recovery with residual nodules in the epididymis is noted in seventeen cases; the subsequent histories of these cases would be of interest. The bacteriological examinations of the pus in the suppurating cases have been given earlier in this paper.

A study of these cases justifies the following conclusions: 1. Epididymitis or orchitis occurring in the course or during the convalescence of typhoid fever is a rare lesion and is of typhoidal origin. 2. Only very exceptionally it is due to secondary microbic infection. 3. It develops at a late period in the disease or during convalescence. 4. The lesion, although as a rule unilateral, may be bilateral, and involves either the epididymis or testicle or both, and not infrequently the cord. 5. Effusion into the tunica vaginalis is rare. 6. Termination most often is by resolution. 7. Suppuration occurs in 25 per cent. of all cases. 8. Localized necrosis and extrusion of testicular tissue is not uncommon. 9. Exceptionally there is destruction of the entire testicular structures. 10. Atrophy of the testicle occurs, but is a rare sequence. 11. The lesion gives rise to little constitutional disturbance. 12. Death as a direct result of the lesion has not been noted.

Notes on 206 Operations for Stone.—ADAMS (*British Medical Journal*, May 25, 1901) states that the operation of choice is lithotrity unless one of the following contraindications prevents: In boys (1) when there is marked cystitis, lithotomy drains the bladder and cures both diseases; (2) when there is much difficulty in passing instruments; (3) when the stone is too large or hard for the necessarily small lithotrite; (4) when there are indications of advanced kidney disease or great debility, the shock of the cutting operation seems less severe, probably because it is briefer. In men (1) when the instruments cannot be passed; (2) when the stone is too large or cannot be grasped. The author has never found a stone too hard. A former operation often renders the introduction of instruments difficult. Lithotrity was successful in the smallest boys. Forty-eight cases were in boys under ten years of age. Only one death occurred in a boy, aged three and one-half years, whose bladder was full of calculi, weighing in all seven drachms. Fifteen of these cases were in children under three years of age, and all did well. Three of the thirty-six cases of lithotomy and three of the 161 cases of lithotrity died. The author concludes with this brief table of cases: With calculi extracted through the meatus, 4; urethral calculi extracted by external urethrotomy, 2; vesical calculi removed by lithotrity (males, 153; females, 8), 161; vesical calculi removed by perineal lithotomy, 36.

The Surgery of Gastric Ulcer.—ANDREWS (*Chicago Medical Recorder*, May, 1901) states in conclusion: (1) Gastric ulcer is a surgical disease; (2) perforating ulcer should be treated by laparotomy as early as possible; (3) bleeding gastric ulcer should be treated by operation after resisting medical treatment; (4) gastric ulcers produce and are also caused by pyloric obstruction, and this calls for operation. Many obscure and obstinate stomach troubles are caused by this cicatricial obstruction, and can be cured very safely by surgical intervention.

THERAPEUTICS.

UNDER THE CHARGE OF

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Treatment of Tuberculosis by Climate.—DR. C. THEODORE WILLIAMS opened the discussion on this subject at the recent British Congress on Tuberculosis. The main points at issue are: (1) What influence has climate on the treatment of tuberculosis? and (2) how far can cases be grouped for treatment in certain climates? Both of these questions he discussed very fully. The belief that has existed in all ages that the disease is curable by climate is, he thinks, justified by the results of such treatment. Under what climatic conditions, he asks, is arrest of the disease most common? What are the real causes of such improvement, and how can they be successfully brought into play? In all climatic treatment, of course, care must be taken to bring the patient fully under the influence of the atmosphere, and to ensure a strictly open-air life by day and by night, with complete hygienic and sanitary surroundings, whether in a sanitarium or elsewhere. But all climates favoring an open-air life are not necessarily suitable for the treatment of consumption; tropical lands must be excluded, because there the appetite is diminished, the nervous and muscular energy depressed, excessive action from the skin induced, and requisite exercise prevented. Bacillary increase is probably also favored. Very moist climates and those in which the sun is often obscured by mist and fog, even though mild, are undesirable, as sunshine is of the greatest importance to the consumptive. The climate which best fulfils the conditions for open-air treatment need not be a very warm nor a very cold one, but should be dry and stimulating, with abundant sunshine, admitting of much exercise and producing nervous and muscular vigor. Climates, he said, must first be classified before they are described, and though it would be possible to arrange them scientifically on the basis of meteorology, as attempted in the Lumleian lectures before the College of Physicians, for the purposes of this discussion a few practical groups will be preferable. These are (1) marine climates; (2) dry, warm climates, partly inland and partly marine; (3) mountain climates. Marine climates include (*a*) the British and Irish seacoast resorts; (*b*) the warm marine climates of Madeira, Teneriffe, and the West Indies; (*c*) sea voyages. Dry, warm climates, the desert climates, and those of the Mediterranean basin, differing in many particulars, but both characterized by warmth and dryness. Mountain climates, characterized by the influence of diminished barometric pressure. The climates discussed were those more easily reached from England. He

spoke particularly in praise of extended sea voyages, especially voyages to Australia and New Zealand and around the Cape of Good Hope in clipper ships. They are most beneficial (1) in cases of hemorrhagic phthisis where large hemorrhage accompanies small areas of tuberculization; (2) in scrofulous or strumous phthisis, where lung disease is accompanied by strumous gland or joint affections; (3) in cases of chronic cavity, where the tuberculous disease is unilateral and quiescent. To ensure the success of a sea voyage the patient must be certain of (1) good and abundant food; (2) proper cabin ventilation; also (3) that the cruise be principally in temperate climes and not in tropical. Of the dry, warm climes the Egyptian desert is highly recommended. With reference to the Riviera, the cases which do best are (1) phthisis in which inflammatory processes have played a large part in predisposing to the disease; (2) strumous phthisis; (3) laryngeal phthisis; (4) unilateral pulmonary tuberculization rather than bilateral; (5) the large class of consumptives who either from extent of disease or feebleness of circulation, or advancing years, are unable to endure the rarefied atmosphere and cold of the high altitudes. Most of these patients love warmth, and cannot take enough exercise when the thermometer is below zero to maintain it. With reference to mountain climates, his conclusions were as follows: 1. The respiration of the rarefied atmosphere produces hypertrophy of the healthy lung and local pulmonary emphysema around the tuberculous lesions, giving rise in due time to thoracic enlargement. 2. It is possible the arrest of tuberculous disease is at least partly due to the pressure exercised in the tuberculous masses by the increasing bulk of the surrounding lung tissue, which, by emptying the bloodvessels, promotes caseation and cretefication of the tubercle. 3. These changes are accompanied by general improvement in digestion and assimilation, the cessation of all symptoms of disease, the return of natural functions, by gain of weight, of color, of nervous and muscular activity, and of respiratory and circulatory power. 4. Arrest of disease takes place in 58 per cent. of the tuberculization cases, and great improvement in 87 per cent. In excavation cases arrest occurs in 21 per cent. and great improvement in 61 per cent. 5. The climate is especially beneficial in hemorrhagic phthisis and phthisis in which hereditary predisposition is strongly marked, and is well suited to chronic tuberculosis of the lungs in general, provided the extent of lung involved is not too large nor the disease accompanied by much fever. 6. Males and females seem to do equally well and to profit most between the ages of twenty and thirty. Males over forty and females under twenty benefit least. 7. The climate is contraindicated in acute phthisis, catarrhal phthisis, in laryngeal phthisis, in cases of phthisis accompanied by great nervous irritability in patients with double cavities, with fibroid phthisis, and in all patients whose pulmonary surface has been so much reduced from any cause that it does not suffice for complete respiratory purposes.—*British Medical Journal*, 1901, No. 2117, p. 198.

Classification of Cases of Tuberculosis and Climatic Treatment—Dr. Burney Yeo discussed this subject in an able manner. He said that the main objects of treatment in pulmonary tuberculosis are (*a*) to arrest catarrhal conditions of the air-passages; (*b*) to improve nervous and circulatory tone; (*c*) to increase the activity of the digestive functions, and thus stimulate

nutrition by promoting the desire and increasing the power to take exercise; (*d*) to raise the moral tone—by no means an unimportant matter—by affording a clear, bright, and cheerful environment; (*e*) to diminish by its asepticity bacterial activity. It must be a question for consideration whether the so-called "open-air treatment," without regard to suitable climatic conditions, will do all this. It should be the object, when practicable, to place the consumptive patient under conditions and in circumstances where, without risk or injury, he may obtain the most complete and perfect aeration of the lungs possible. The difficulties in the way of finding suitable abiding places for the tuberculous were pointed out, and Dr. Yeo cited some marvellous "cures" which occurred in patients who never left London. Many chronic stationary cases with fair general health travel about to different winter resorts with successive seasons, and take no harm in doing so. The answer to the first part of the question, he suggests, will be that a suitable climate (*a*) relieves or removes the catarrhal conditions accompanying the disease in a number of cases; (*b*) it raises nervous and vascular tone; (*c*) it increases muscular energy and the ability as well as the desire for exercise; (*d*) by rendering an open-air life possible it increases the aëration of the lungs and diminishes the activity of the bacterial agencies, one of the most essential conditions of arrest and cure of the disease; (*e*) it improves the tone and promotes the activity of the digestive functions, and so enables the patient to take the large amount of food which is needed to heighten his state of nutrition; (*f*) and, finally, it improves the moral and mental state by surrounding the patient with a bright, cheerful, and hopeful environment. Then, as the answer to the second part of the question, he says: 1. Cases seen at the very commencement of the disease, and which are otherwise in good health, may be permitted a certain amount of choice in the selection of a climate, provided it allows of many hours being spent daily in the open air, and that they are placed under admittedly hygienic conditions. A choice may be made from climates of altitude, the desert climate, the inland plateaux of South Africa, the sea voyage for those with a decided liking for the sea, and suitably placed sanatoria. 2. For progressive febrile cases, repose in bed or on a couch at home, in the best conditions practicable for the free access of air and sunshine to their apartments. 3. For advanced cases home is best if the conditions of home-life are favorable, or the warm marine climates, with cheerful surroundings, if home life is unfavorable or change is urgently desired. 4. For catarrhal cases warm, soothing climates, like Madeira or Teneriffe, are best. 5. For rheumatic or gouty cases of the fibroid or pleurogenic type—dry, marine climates or the desert climate are most suitable. 6. For the so-called "scrofulous cases," if free from catarrh, fairly bracing marine climates; if with catarrh, mild marine climates should be prescribed. 7. For most other moderately advanced cases, with the limitations already mentioned, the climate of the high mountains, above the cloud belts, is the most curative.—*British Medical Journal*, 1901, No. 2117, p. 202.

Treatment of Cholera Infantum.—Dr. W. Blair Stewart states that climatology and diet are two of the most important features in the treatment of cholera infantum. If the means of the patient will afford it, send the child from the close room to the seashore, to live in the open air. Sea air

with slight assistance from medicines will work many cures in apparently hopeless cases. The earlier in the attack the child is sent to Atlantic City or to other healthful seaside resort the greater its chance of recovery. If circumstances do not permit of such a trip, place the child in the coolest room of the house, where free ventilation can be obtained; or, what is much better, on a cool porch. Do not nurse the child in the arms, but place it on a cool, solid bed, where all motion can be avoided. Never rock the child in a cradle. Always starve these patients the first twelve to thirty-six hours. If the child is breast-fed do not allow too frequent nor too prolonged nursing. This class of patients is the easiest to manage. In bottle-fed babies you will have your troubles. After the preliminary fast begin with teaspoonful doses of barley, albumin, or toast-water, and as this is well retained add small quantities of the best pure fresh milk mixed with lime-water until the normal feedings can be borne. Many times it may be necessary to resort to some good prepared food in very small quantities where milk is not tolerated in raw or predigested form. Try a weak lamb, mutton, or beef broth (absolutely free from grease and pepper) at first, and gradually add to this pure expressed beef juice, always watching to avoid too frequent or overfeeding. Do not try solid foods in older children until several days after all symptoms have subsided. These are good general rules or outlines of treatment, subject to change in each case. Their neglect will usually lead you into trouble. Make an exhaustive physical and dietetic study of each case, and remember that elimination is first, diet is second, hygiene and change of air third, and antiseptics and astringents are last in therapeutic importance.—*International Medical Magazine*, 1901, vol. x. p. 389.

Atropine in Ileus —Much literature has recently been published concerning the life-saving properties of atropine in desperate cases of intestinal obstruction of various kinds. Dr. H. Gebele raises a warning cry against the too free use of this remedy, since it too often obscures the clinical picture, and, far from being infallible, it prevents the surgeon from selecting the proper moment for operation. It is only in the paralytic or spastic form of obstruction that internal treatment has any effect, and here small doses of morphine have the same effect as atropine, and are to be preferred. In mechanical obstruction atropine is still less indicated, and gastric lavage, enemata of several quarts of olive oil, or of castor oil, and, above all, operation must be resorted to.—*Münchener medicinische Wochenschrift*, 1901, No. 33, p. 1313.

Therapeutic Uses of Scopolamine Hydrobromate.—Dr. M. Rosenfeld, working in the Psychiatric Clinic at Strassburg, finds that this drug has a decided action on the normal as well as the sick individual. Dosage depends largely on the age, condition, and strength of the patient, but on the average one two-hundredth to one one-hundredth grain, thrice daily, is sufficient. It acts as a strong sedative in the insane, and also in those with minor nervous disorders, as hysteria and neurasthenia. Certain by-effects, such as dryness of the skin, itching, slight dizziness, were noted, but should not be considered contraindications to its employment. It is essential to use fresh solutions, since a decomposition of the drug takes place in old preparations.

Injections are best borne immediately after eating, and, as no cumulative effects have been noted, may be continued for long periods of time.—*Therapie der Gegenwart*, 1901, vol. vii. p. 298.

Treatment of Chlorosis.—Dr. Gustav Fuetterer concludes a short study of this subject as follows: (1) That great attention should be given to the study of chlorosis clinically; that clinical observation should be controlled by taking the specific gravity of the blood; that a very energetic treatment, mainly with beef juice properly prepared, should be instituted at once and continued until the specific gravity of the blood has become normal; (2) that chlorosis or secondary anæmia in tuberculosis must receive the same consideration and treatment, no matter what other treatment may be employed; (3) that it is advisable to cause an artificial anæmia in animals to be inoculated with suspected tuberculous sputum, for diagnostic purposes, as a finer reaction will take place, and more accurate and probably quicker results can be expected; (4) that chlorosis in early years, or secondary anæmia in later years, allows a round ulcer of the stomach to form and prevents its healing, while the presence of a normal or nearly normal percentage of hæmoglobin brings prompt repair, and that, therefore, chlorosis or secondary anæmia, coexisting with round ulcer of the stomach, should receive our first attention before any so-called ulcer treatment is instituted. While a very high opinion of the effectiveness of a rest-cure in cases of ulcer of the stomach is to be entertained, a preparatory treatment with beef-juice brings much better results; (5) that therapeutic measures, as described in this paper, particularly fresh and properly prepared beef-juice, allow us to create a normal composition of the blood, both in chlorosis and in secondary anæmia, as a rule, in a very short time.—*Chicago Medical Recorder*, 1901, vol. xxi. p. 1.

Vioform.—The many substitution-products of iodoform have not been able to leave a lasting impression, with the sole exception of vioform, says Dr. D. Krecke. It not only possesses the great advantage of iodoform, of keeping wounds absolutely dry and free from germs, but it is almost as great a specific as this in tuberculous processes, and lacks any disagreeable odor. Vioform is capable of replacing iodoform in all respects in rectal and vaginal surgery, as well as in operations about the mouth and other places where contamination of the wound surfaces is unavoidable. In tuberculous joints suppuration is apt to follow vioform injections, so that it is not recommended so highly here.—*Münchener medicinische Wochenschrift*, 1901, xlviii., No. 33, p. 1310.

Gelatin as a Hæmostatic.—The technique of the employment of gelatin for increasing the coagulability of blood is described by Dr. J. Sailer as follows: The gelatin is prepared as for ordinary media, using, however, five to eight hundredths of 1 per cent. saline solutions instead of bouillon. Since the degree of pain experienced on injection seems to be proportionate to the amount of turbidity, it is important to thoroughly clarify the solution with white of egg. Sterilization is then accomplished by heating in an ordinary steam sterilizer fifteen minutes for three successive days. In regard to the strength of the solution, there seems to be considerable divergence of

opinion. Generally, however, 5 to 10 per cent. solutions are employed locally, and 1 or 2 per cent. for subcutaneous injection. About ten ounces of the 1 per cent. solution are usually required. The preferred situations for injections are between the shoulder-blades, under the breast, and on the outer side of the thigh. They are indicated in all hemorrhages, such as hæmoptysis, hæmatemesis, metrorrhagia, melæna neonatorum, purpura, and the purpuric forms of the infectious diseases, and are contraindicated in only one condition, viz., acute nephritis.—*Therapeutic Gazette*, 1901, vol. xxv. p. 508.

Euchinine a Prophylactic in Malaria.—Dr. A. Mori reports that euchinine in doses varying from four to eight grains a day is capable of preventing malaria in those not protected by living in mosquito-proof houses. It is advisable to begin treatment four or five months before the usual malarial season. He reports, further, that in a series of observations on eighty-nine individuals under similar circumstances that in forty-two who had been under treatment only five contracted malaria, while in forty-seven who were not so treated thirty-nine suffered. The five who contracted the disease had it in a mild form.—*Centralblatt für Bakteriologie*, 1901, No. 20, S. 786.

Sero-therapeutics of the Plague.—Dr. John Brownlee gives a series of personal experiences in the use of the Yersin plague serum in the recent cases at Glasgow. With reference to its prophylactic action, he says that this serum did not convey absolute immunity in the cases under observation, but that if the disease is established, after its use, it is liable to be much less severe. From the stand-point of its curative action he holds that the subcutaneous use of the serum is not of any great curative value.—*The Lancet*, 1901, vol. clxi. p. 435.

Treatment of Syphilis by Injections.—Dr. M. Stern says that the disadvantages of the usual inunction treatment of syphilis are many. The most important are uncleanliness, inexact dosage, and the frequency with which the cure is interrupted by the patients themselves, the result being the present increase of tertiary and parasyphilitic affections. Injection, on the other hand, is convenient and easy of administration, rapid in action, and possesses the further advantage that the physician need not leave the greater part of the treatment to the discretion of the patient. In cases in which there is a diseased or senile skin the absorption of mercury is much diminished, and injections become a necessity; when a rapid diagnosis has to be made they are far superior to inunction. Concerning the use of insoluble or soluble mercurials opinions are divided, but the former possess the advantages that they have to be given less often, and that from six to ten injections generally suffice. The author has tried the various salts and combinations recommended, and finds that calomel generally causes too intense pain, while gray-oil injections are liable to be followed by infiltrations and abscesses. The best results have been obtained by him with sublimate.—*Münchener medicinische Wochenschrift*, 1901, vol. xlviii., S. 1084.

OBSTETRICS.

UNDER THE CHARGE OF

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Protargol in Ophthalmia Neonatorum.—PIOTROWSKI (*Centralblatt für Gynäkologie*, 1901, No. 31) has employed protargol in varying solutions in a large number of cases for catarrh of the conjunctiva. The result of his experiments has been the adoption of the following method: Immediately after labor the lids are cleaned with 3 per cent. boric acid solution and the eyes thoroughly irrigated with 10 per cent. solution of protargol. Secondary catarrhs have not followed this practice, and it has proven thoroughly satisfactory.

Rupture of the Symphysis.—RUTH, from the clinic at Riga, reports in the *St. Petersburger Medicinische Wochenschrift*, 1901, No. 24, the case of a patient who had borne a child and gave a history of uninterrupted health. In her second labor she was attended by a midwife, who examined her without antiseptic precautions. As birth did not proceed, the midwife endeavored to pull out the head with her hands, and, failing in this, physicians were summoned, who delivered the child with much difficulty by the use of forceps. There was an extensive laceration and hemorrhage. The patient became septic, and in this condition was seen by Ruth.

On examination the bladder was found intact. The lacerations had not healed. An abscess was found behind the symphysis, and a fistula leading thence into the connective tissue of the pelvis. The symphysis had been ruptured extensively. The abscess was opened and drained, the patient freely stimulated, but succumbed to septic infection. At autopsy the septic process was independent of the rupture of the symphysis, and no direct connection could be traced between the abscess cavity and the joint.

Contributions to the Pathology of the Newborn.—In the *Comptes Rendus de la Société d'Obstétrique, de Gynecologie et de Pediatrie de Paris*, 1901, vol. iii., PORAK and KATZ report the case of an infant, about one month old, born in spontaneous labor, who had after birth intense icterus and failing respiration. Convulsions supervened, limited to the face and eyes. The child died in a convulsion. Upon examination an extensive cerebral hemorrhage limited to the right ventricle was found. It seemed most probable that an acute infection was the cause of the hemorrhage.

Softening of the cerebral hemisphere in a nursing infant was also observed in the case of a child born in the eighth month of pregnancy and delivered in an easy labor. The child had no symptoms pointing to cerebral disease, and seemed to perish from weakness. It lived thirty-six days after birth.

A congenital diaphragmatic hernia was reported by the same observers in a child born of a multipara strong and healthy. The child presented no apparent malformation, breathed badly, became rapidly cyanosed, and perished. It was noticed that the apex of the heart beat upon the right side instead of upon the left. In the left half of the chest there was resonance over a greatly distended intestine. Upon autopsy the left half of the chest was filled with the intestine. The left lobe of the liver was behind the costal cartilage. The stomach, duodenum, pancreas, and spleen were also within the thoracic cavity. This rare condition could not be traced to violence, and must be considered as a congenital malformation.

Fatal Poisoning with Bichloride of Mercury.—La Page (*Comptes Rendus de la Société d'Obstétrique, de Gynecologie et de Pediatrie de Paris*, 1901, vol. iii.) reports the case of a woman who had an abortion and in whose case it was proposed to curette the uterus and douche it with a solution of carbolic acid. By mistake a strong solution of bichloride of mercury was allowed to run through a catheter into the uterus. The womb was at once washed out with sterile water and packed with gauze.

The patient speedily developed suppression of urine, mercurial diarrhœa, and delirium, and died. An autopsy could not be obtained. Before death she suffered greatly from irritability of the bladder, diarrhœa with tenesmus, and exceedingly fetid discharges.

[This case may serve as a reminder that bichloride of mercury is an unsafe substance to introduce within the uterus. In ordinary dilutions its employment has been followed by fatal absorption.]

Extra-uterine Fœtation.—Malcolm (*British Medical Journal*, July 13, 1901) describes his experience in cases of extra-uterine fœtation. He draws attention to the fact that the fœtal bones may be retained for a long time with comparatively little injury, and describes the case of a patient upon whom he operated for ovarian tumor, removing at the same time the bones of a fœtus that had died seven years before. They lay between the ovarian cyst and adherent coils of small intestine, and could not be left. He compares the growing ovum to an ovarian tumor developing deeply between the folds of the broad ligament, and those anatomical relations which the operator will find are much the same in the two cases. As illustrating the obscurity of diagnosis with many of these patients, he describes the case of a woman, married twenty years and having two children, the younger eighteen years old. She had discharges from the uterus and irregularities of menstruation for fifteen or sixteen years. She had been seized with sudden illness some weeks before coming under observation. Upon examination a large mass was found in the pelvis, and when the febrile symptoms and pain abated a rounded tumor was found fixed in the hollow of the sacrum. Upon operation the mass was a collection of blood, due to the rupture of the Fallopian tube.

Rupture of the Uterus in a Multipara.—Simpson (*British Medical Journal*, July 13, 1901) reports the case of a woman, illegitimately pregnant, who was taken in labor when alone. When seen the patient was dying, the

stump of the child's right arm was protruding from the vulva, and the forearm had been separated with a breakfast knife. The patient soon died.

Upon examination the child and placenta were found in the peritoneal cavity, with the exception of the stump of the right arm and the head. Rupture of the uterus four inches in length was found upon the left side, where the peritoneum was reflected to form the broad ligament.

The rupture probably occurred by vigorous movements of the fœtus occasioned by the mother, who cut off the forearm as it presented in a desperate attempt to conceal her illegitimate pregnancy. This caused a strong reflex action of the child, which plunged its feet through the uterine wall, rupturing the uterus and dragging the placenta with it.

Rupture of the Uterus in Placenta Prævia.—MAXWELL (*British Medical Journal*, July 13, 1901) recently reported before the Obstetrical Society of London three cases of rupture of the uterus in placenta prævia. In the first the woman died undelivered within a few minutes of the rupture. In the second the uterus was found ruptured posteriorly. After delivery the patient had dangerous hemorrhage, but recovered after gauze packing. The third case was as follows:

The patient was a primipara in poor health during pregnancy. She had weak uterine contractions, and the cervix dilated slowly. The edge of the placenta was felt posteriorly, and there was some hemorrhage. Labor passed by and returned fourteen days afterward, when free hemorrhage occurred, from which the membranes ruptured, the child's head coming down. Gentle pressure was made upon the uterus as the head descended. The child was born without assistance in ten minutes. Very free hemorrhage followed until the placenta was delivered and the uterus compressed. It was found that the bleeding came from a rent in the posterior wall of the uterus and cervix, and the fingers could be passed directly into Douglas' pouch. This rent was packed with gauze and pressure maintained upon the womb. The patient made a recovery without infection. The child weighed but five pounds, was puny, and died of pneumonia three weeks after birth. The placenta was marginal, and rupture had occurred through the entire cervix and lower portion of the placental site. These cases occurred in Chinese women.

In discussion the treatment was indorsed, and Herman expressed his doubt that the uterus is softened in placenta prævia as often asserted. Spencer had employed gauze packing in rupture of the uterus with success, and believed it much better than abdominal section and hysterectomy. Routh had seen one case of spontaneous rupture of the uterus with placenta prævia. The patient was eight months pregnant, and had several attacks of hemorrhage. Under deep anæsthesia the cervix was rigid, and it was not easy to insert the finger. An anterior marginal placenta was found. The tongue of the placenta was separated from the lower uterine segment, podalic version was performed, and the leg brought down and the child left for natural delivery. After twenty-four hours the child and placenta were spontaneously expelled. The patient became septic, and upon examination it was found that the uterus had ruptured anteriorly. The patient died. Horrocks had seen a most extensive rupture of the uterus treated by packing,

which was renewed under chloroform every day for twelve days in succession, and then less frequently. The patient at last expelled a large slough from the right broad ligament, and ultimately recovered.

GYNECOLOGY.

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Primary Tuberculosis of the Genital Tract.—BERNHEIM (*La Gynécologie*, 1900, No. 5) in a paper on this subject summarizes as follows: 1. Tuberculosis of the genital tract in the female is not rare, as would be proved if a systematic bacteriological examination of all vaginal discharges were made. 2. The disease is most common in women between the ages of eighteen and thirty, although it has been observed in old women and infants. 3. Infection occurs during coitus, through the medium of foreign bodies, syphilitic lesions, etc., in an individual predisposed to the disease. 4. The tubes and ovaries are most often affected, less frequently the uterus, vagina and vulva. 5. Whenever a uterine trouble is not clearly of inflammatory origin, the possibility of tuberculosis should be borne in mind. 6. When other microorganisms beside the tubercle bacillus are present and suppuration is probable, the only treatment is surgical.

Regeneration of Ovarian Tissue.—KANEL (*Wratch*, 1900, No. 13) examined ovaries of rabbits between two and three weeks after they had been subjected to mechanical and other injuries. His conclusions are as follows: 1. Aseptic wounds heal rapidly without the formation of granulation tissue, nor is there any evidence of local congestion and diapedesis such as usually accompanies the process of repair. 2. The primary healing is due to the activity of the epithelium of the medullary layer. 3. Lesions due to irritation of the ovary with turpentine result in the formation of cicatricial tissue which develops from the fibrous tissue of the stroma. 4. Infection with the staphylococcus albus is accompanied by extensive formation of granulation tissue and necrosis, with the subsequent appearance of a large cicatrix.

Prognosis and Treatment of Uterine Fibromyoma.—TORRE (*La Gynécologie*, 1900, No. 5), in a paper read before the last International Medical Congress, concludes that uterine fibroids are to be regarded as purely benign in character, their seriousness being due only to the changes which they may undergo and to the clinical symptoms. Normal pregnancy and par-

turition are often possible in a myomatous uterus, hence the attempt should always be made to spare the organ if possible.

In the absence of symptoms there is no indication for treatment. Hysterectomy is a last resort, to be confined to cases in which no other treatment is practicable. It is irrational to adopt this course in every instance.

CULLEN (*Ibid.*), in discussing the same subject before the Congress, calls attention to the fact that when the tubes and ovaries are healthy the endometrium is normal, and, on the other hand, the uterine mucosa is diseased when there are morbid changes in the adnexa. He is strongly in favor of preserving a portion of the uterus, even when large tumors were removed, and prefers the vaginal route in every case. Ligation of the uterine arteries he regards as an unscientific procedure on account of their free anastomosis with the ovarian arteries.

Methylene Blue in the Treatment of Endometritis.—CHALEIX-VIVIE and KOHLER (*La Gynécologie*, 1900, No. 5), as the result of a series of clinical experiments with methylene blue, pure, in concentrated solution and in the form of powder, affirm that it is a valuable remedy in cases of uterine hemorrhage and leucorrhœa, and has a marked analgesic action in dysmenorrhœa associated with disease of the endometrium. It is also useful in cases of disease of the adnexa and old hæmatoceles. Its bactericidal action has been proved by numerous experiments.

Intraperitoneal Shortening of the Round Ligaments.—SCHWARTZ (*Transactions of the Thirteenth International Medical Congress*) prefers this method to hysteropexy, although nine out of sixty-three patients on whom he performed the latter operation subsequently bore children. He regards it as a more scientific procedure, less apt to be followed by trouble during pregnancy and parturition.

STANKIEWICZ (*Ibid.*) believes that every case of retroflexion during the period of sexual activity should be treated, preferably by pessaries, though he notes only three cures in 109 cases. Surgical intervention offers the best prospect of a permanent cure. He prefers the method of intravaginal shortening of the round ligaments, recommended by Bode and Wertheim, with some modifications. In twenty-seven cases 87.5 per cent. were successful. The advantages over the Alexander operation are: 1. The avoidance of hernia. 2. Both ligaments may be shortened through a single incision. 3. The ligaments can invariably be found. 4. The method is applicable to cases of adherent retroflexion. 5. Diseased adnexa can be treated at the same time. 6. The results are entirely satisfactory. 7. There is no visible cicatrix or subsequent pain.

Ligation of the Uterine Arteries in the Treatment of Uterine Fibroids.—GOTTSCHALK (*Transactions of the Thirteenth International Medical Congress*) reports the ultimate results of this operation in his practice, extending over a period of twenty-two years. In all but three cases the results were satisfactory. His technique is briefly as follows: After separating the cervix, as in the first step of vaginal hysterectomy, he ligates the base of each broad

ligament, using three or four ligatures of strong silk. The operation is followed by no reaction, even in the case of weak and exsanguinated patients who could not survive a radical procedure. It is especially recommended as a palliative measure in cases of profuse hemorrhage, but they must be carefully selected. The most favorable are those of interstitial tumors in the lower or middle segment of the uterus, those at the fundus being less amenable to this treatment, while the intraligamentary variety is entirely unsuitable. The tumor should not exceed in size the fœtal head at term. The nearer the menopause the better is the prospect of a permanent cure. If the patient's history and symptoms point to a previous attack of peritonitis, with resulting vascular adhesions, the prognosis after ligation of the uterine arteries is uncertain.

Treatment of Cancer of the Uterus.—BOUILLY (*La Gynécologie*, 1900, No. 5) concludes a paper on this subject, with the statement that in his opinion abdominal hysterectomy for cancer of the uterus will continue to be employed in a few carefully selected cases in which it is desirable to remove some of the most accessible lymph nodes. Vaginal hysterectomy should be practised in cases in which the disease is limited and the operation easy, or when the patient is old or unusually stout. Neither of the operations is to be regarded as of positive value, though a few positive cures have been recorded. Curettement is of great benefit in cases that are unsuitable for a radical operation.

Etiology of Cancer.—LEOPOLD (*La Gynécologie*, 1900, No. 5) concludes from a series of experiments that pure cultures of blastomycetes may be found in fresh cancer of the ovary. After injecting this culture into the testicle of a rat it soon died, and its peritoneum was found to be studded with nodules in which were masses of blastomycetes, which in their turn furnished pure cultures. Hence the inference that these may be the cause of malignant disease in man and are capable of inoculation in the lower animals, causing the development of similar growths.

Shortening the Round Ligaments.—EBERLIN (*La Gynécologie*, 1900, No. 5) believes, as the result of his own and others' observations, that this operation is the most rational one yet devised for the cure of movable retroflexion, and that with a proper technique it is invariably successful. The only way to certainly find the ligament is to open the inguinal canal.

Pregnancy and parturition do not affect the ultimate result, nor is there any danger of hernia when the different layers of the wound are accurately sutured. In order to avoid this complication and to insure success it is highly important to strip back the peritoneum at the internal ring.

Large Dermoid Cyst in a Child.—MCKEE (*University Medical Magazine; Frauenarzt*, April 19, 1901) reports the case of an immense abdominal tumor in a girl, aged seven years, which, on account of its rapid growth, shape, consistence and location (in the left renal region), was considered to be a sar-

coma of the kidney. At the operation a large kidney-shaped dermoid cyst of the left ovary was found.

The reporter concludes that in a case of large abdominal tumor in a young child the possibility of ovarian dermoid should be borne in mind. The diagnosis will be aided by examination under anæsthesia or an X-ray picture. An explorative incision is indicated.

Origin of Dermoid Cysts of the Ovary.—BANDLER (*Archiv für Gynäkologie*, Band lxi., Heft 3) concludes an elaborate paper by affirming that he has no doubt that ovarian dermoids originate from the Wolffian body and duct, as do some other cysts of the ovary and broad ligament. All the glandular structures spring from the included ectoderm. No real trace of an organ is ever found, and what has been described as gliomatous tissue, if it is really such, is only a product of the ectoderm.

Tenotomy of the Sphincter Ani in Perineorrhapy.—FRITSCH (*Centralblatt für Gynäkologie*, 1901, No. 2) formerly used a piece of rubber tubing to allow the escape of gas after operations for complete laceration, as well as to overcome spasmodic contraction of the muscle during the healing process. He now adopts Simon's suggestion, to divide the sphincter posteriorly, but does this after instead of before the operation. The tip of the left index finger is inserted into the anus, and if the opening is found to be too narrow subcutaneous incision of the muscle is practised with a curved tenotome, the finger acting as a guide to protect the bowel. It is better to make two incisions, one on either side of the median line posteriorly, about half an inch apart. Then a piece of rubber tubing wrapped in iodoform gauze is introduced to the depth of two inches. The pain usually accompanying the subcutaneous incision is slight, and the sphincter regains its function perfectly.

The writer adds that catgut is not the best material for buried suture of the sphincter and levator ani muscles. He prefers fine linen thread, as suggested by Pagenstecher.

Paraffin Injections in Incontinence of Urine.—GERSUNY (*Centralblatt für Gynäkologie*, 1900, No. 48) reports a case of incontinence complicating gonorrhœal vaginitis, in which under cocaine anæsthesia he injected paraffin ointment beneath the everted mucous membrane at the neck of the bladder. Similar injections were made about the meatus. A firm ring was formed around the vesical orifice which completely closed it, as was shown by injecting water. Two hours later a catheter was passed, and it was necessary to empty the bladder in this way for twenty-four hours, no dribbling having occurred in the meantime. As the incontinence returned the paraffin injections were repeated a week later, which resulted in severe tenesmus during the next two or three days, but five days after the second operation the patient was able to retain her urine for an hour and a half. When examined three weeks later the ring of paraffin around the neck of the bladder was unchanged.

Three months after the last injection the patient reported that she could retain her urine from four to six hours, and had no dribbling on exertion. The cure was permanent.

OPHTHALMOLOGY.

UNDER THE CHARGE OF

EDWARD JACKSON, A.M., M.D.,
OF DENVER,

AND

T. B. SCHNEIDEMAN, A.M., M.D.,
PROFESSOR OF DISEASES OF THE EYE IN THE PHILADELPHIA POLYCLINIC.

Tobacco Amblyopia in Daily Practice, with Analysis of Fifty Consecutive Cases.—KERR (*Quarterly Medical Journal for Yorkshire, etc.*, May, 1901) calls attention to the salient symptoms of tobacco amblyopia as contrasted with other conditions leading to poor vision, based on an analysis of fifty cases. Bright's disease, tabes, cataract, and simple glaucoma are to be excluded. Any of these diseases may complicate the toxic amblyopia.

Tobacco amblyopia occurs generally in men from forty-five to fifty-five. One of his cases was only twenty-six, in a man who had smoked at least half an ounce thick twist daily for two years. Another occurred in a man, aged eighty-six years, who had smoked a similar amount for many years. Patients are generally smokers of three ounces or more weekly of the coarse and dark kinds of tobacco, and some use as much as an ounce daily. Many also chew; but it is not a necessary result of even excessive smoking. The disease may come on insidiously or rapidly, in a week or two, as failure of central vision. It is always painless. The visual acuity is very poor, often less than 6/60, and scarcely improved by glasses. In about one-third of the cases some atrophy is noted, the outer half of the disk generally being very pale, and in a few the arteries markedly narrowed. The lesion is at first limited to the macula or the macular bundle of the optic nerve, so that there is at the macula and around it a region where colors are not well recognized, and at the macula itself an exceedingly small area where even white is not distinguished. To detect the scotoma a bit of red one centimetre square is shown the patient. He will fail to recognize its real color. One eye often shows the color scotoma better than the other, apart from differences in the visual acuity of the two eyes.

Tobacco is the cause of the disease, but many debilitating causes may contribute. Alcoholic excess is frequently associated; its importance is probably exaggerated. The Australian horses which eat wild tobacco and become amblyopic are certainly free from alcoholism. Other associations, generally of a debilitating nature, may be present. In one case a blow on the eye seemed to cause the onset, and that eye was the worst. The author thinks hypermetropia too frequent an association to be accidental. One case, with stomach trouble debilitating her, was remarkable as being in a woman, the small amount of tobacco consumed (half an ounce weekly dark shag) and the speedy onset within a year. Relapses are rare.

The treatment is to stop tobacco in every form. The vision may deterior-

ate for a week or ten days; it should soon begin to improve, and in two months very definite improvement should have taken place. Strychnine appears to hasten improvement; it is said, also, to relieve the desire for tobacco. Some, but very few, may, if due to debilitating causes, improve without discontinuing the tobacco as the health improves. It is well to look for tobacco amblyopia as a complication in other ocular diseases. Its discovery may improve the prognosis.

New Method of Muscular Advancement in Strabismus.—FROMAGET (*Journ. de Med. de Bordeaux*, 1901, No. 18) calls attention to the unsightliness of the buckling of the tissues which necessarily results from advancement of the tendons of the recti muscles as usually practised, and to the loss of motility due to the adhesion of the conjunctiva as a bridle in the cicatrix. The ideal should here be not only to straighten the eye, but also to preserve its movements intact. The muscular insertions are to be displaced without the involvement of the conjunctiva. To accomplish this he employs the following procedure: 1. After having tenotomized the retracting muscle he divides the conjunctiva, over the tendon to be advanced, in a vertical curved line, concave toward the cornea, about 4 mm. from the limbus. 2. He then dissects the distal conjunctival flap as far back as possible to disengage the tendon and its expansions. He next dissects the corneal flap of the conjunctiva so as to be able to slide the end of the tendon beneath it according to the degree of advancement desired. 3. An assistant then raises and retracts the distal flap of the conjunctiva. Two sutures are passed through the exposed tendon—one above and one below. The needle is passed into the episcleral tissue and made to emerge near the vertical diameter of the cornea, above and below, exterior to the limbus. The suture thus includes the tendon, the episcleral tissue, and the corneal flap of the conjunctiva. 4. The tendon is then divided on a level with the sclera, care being taken not to cut the sutures. 5. The eye is brought into the desired position by means of fixation forceps in the hands of an assistant, and the two sutures are then drawn tight and tied. The sutures thus include in their knot only the corneal conjunctiva, which readily smooths out later. 6. As to the flap of distal conjunctiva, it is left to smooth itself out and to cover over the operative field. If it is too redundant, enough is resected to make nice contact with the corneal flap. A small superficial conjunctival suture can be applied if thought necessary.

As in the ordinary procedure, the muscle is seized further back and the sutures are brought out nearer to the vertical diameter of the cornea, according as a more decided degree of advancement is desired. The results obtained by this method have been durable and satisfactory from a cosmetic point of view.

The Electric Light in Ophthalmology.—AUBARET (*Journ. de Med. de Bordeaux*, 1901, No. 19) extols the electric light for various diagnostic purposes in ophthalmology (beside its use as a source of illumination in ophthalmoscopy) as in lateral and indirect illumination, exploration of the ocular globe by transparency, and of the sinuses by diaphanoscopy. The test-letters and optometers can be illuminated by electricity, and the mobility

of the muscles can be examined more accurately by the same light. For the illumination of the fundus electric lamps of ground-glass are preferable, giving a more uniform and less intense light. They may be placed behind screens; it is better, however, to surround them with a metallic cylinder having a circular opening 45 mm. in diameter. Such an opening gives light enough. This arrangement emits almost no heat. It constitutes a real advance in the classical technique of ophthalmoscopic examination.

1. The electric light can be attached to the handle of the ophthalmoscope itself, inclining the mirror at 45°. Wolf's method of using the total reflection of a prism is, however, much to be preferred. His very ingenious instrument was shown at the Congress of Ophthalmology. Aubaret makes use of a different plan. He dispenses with the mirror, the light taking its place directly—a small electric lamp enclosed in a metallic envelope having an opening in its anterior part. It may be placed quite close to the sight hole, in front of a plate like that which carries the mirror in an ordinary ophthalmoscope. It can be adapted to any ophthalmoscope. It is not necessary to throw upon the pupil a homocentric pencil, as with the mirror. Both pupils are illuminated at once. Examination with the indirect image is very satisfactory. The fields of illumination and examination are as extensive as by the ordinary method. As a matter of fact, the entire pupil is not utilized, but the pupillary field is the more illuminated the closer the lamp is brought to coincide with the line of sight. Thus examination in the direct image is less satisfactory than in the indirect. The method realizes in a perfect way the primitive disposition of Brücke's experiment. Stilling, who was one of the few to practice orthoscopy, made use of an analogous but less perfect plan. But with the former methods of illumination orthoscopy was useful only in exceptional conditions, such as high degrees of hypermetropia, or detachment of the retina. Thanks to the electric light, it may now rival ophthalmoscopy.

2. Oblique illumination. Lateral illumination is greatly facilitated by the use of the electric light. Aubaret employs two metallic tubes sliding the one into the other, one of which carries the electric lamp and the other a strong converging lens. Any desired degree of convergence of the light can thus be obtained.

3. Illumination by transparency and illumination of the sinuses. Diaphanoscopy of the eyeball requires special forms of illumination. Cylinders of glass permitting the concentration of the rays upon a very small surface are employed as in the apparatus of Birnbacher and Rochon-Duvignaud. Optometric measurements may also be made under very convenient conditions of illumination. Transparent test-letters illuminated by lamps placed behind them permit of measurements comparable with one another. The optometric scales can be illuminated in the same way.

Optometric measurements can also be made in the dark-room, a great advantage, because more perfect relaxation of the accommodation is thus obtained. Finally, a very elongated electric lamp, having somewhat the form of a luminous cylinder, 12 cm. long and 2 cm. in diameter, mounted on a handle, can be readily carried into all parts of the field for examining the condition of the muscles by means of double images. The position of the false images, and especially their inclinations, can be best determined

by this apparatus—a determination very difficult with the ordinary candle. Its light, also, is fixed and immovable and not waving like the ordinary flame, permitting much greater precision and exactness.

Injections of Vaseline after Enucleation of the Eyeball.—DIANOUX (*Gaz. Méd. de Nantes*, 1901, No. 31) recommends the injection of vaseline after enucleation for the purpose of giving the stump a convex shape forward in place of the concavity ordinarily obtained. The injection is practised into the soft tissues in the axis of the orbit to a depth of 5 or 6 mm., after all inflammatory reaction has disappeared. He concludes: 1. That the injection of vaseline is entirely harmless. 2. That any degree of projection desired can be given to the tissues. 3. That the stump thus obtained possesses great mobility. 4. That a radical reform is to be expected in the shape of artificial eyes.

HYGIENE AND PUBLIC HEALTH.

UNDER THE CHARGE OF

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AND

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The Possibility of Infection by Minute Droplets Thrown Out in Speaking, Coughing, and Sneezing.—Bearing on the contention of Flügge, denied by Cornet, that the transmission of pulmonary tuberculosis from one person to another is chiefly by means of the finest droplets thrown into the air in speaking, coughing, and sneezing, the experiments of DR. H. KOENIGER (*Zeitschrift für Hygiene und Infectionskrankheiten*, xxxiv., p. 119) are of interest. In order to give the expelled droplets a character which would enable them to be traced, he rinsed his mouth with liquid rich in *B. prodigiosus* or *B. mycoides* or with very dilute caustic soda. When the bacteria were employed, Petri dishes were exposed at different heights and distances, but when the alkali was used in place of the Petri dishes, glass plates coated with phenolphthalein were exposed. Since this agent turns pink when an alkali is brought in contact therewith, this method enables one to determine not only the number of the droplets, but their size as well. Shortly after rinsing the mouth and rejecting the surplus, he would take a position in a room, avoiding as much as possible unnecessary stirring up of the air, and then speak, sneeze, and cough. After an interval the number of colonies was determined. Tests were made with single letters, with different kinds of speaking by the same person and by different persons—loud, soft, and whispering—and to determine the influence of rapidity. It was found that no droplets are thrown out in ordinary exhalation, nor in vowel formation, while the number is very great with consonants, as *t*, *k*, and *p*, which

originate by the sudden release of air under pressure in the mouth cavity, the number depending upon the amount of force with which it is released, and hence largely proportionate to the manner of pronouncing and to the sharpness of consonant formation. Loudness and rapidity have but little influence; indeed, whispering may, under some conditions, cause a greater number of droplets than loud speech. Even with subdued speech and a quiet atmosphere, it was found that the organisms expelled penetrated into the farthest parts of the room, which was over twenty feet in width, and not alone forward, but sideways and backward from the speaker. The bacteria were found not to remain in supension in the air longer than an hour, and it was noticed that they fell upon the plates in groups, sometimes as many as forty close together. This suggests that the bacteria in the droplets do not fall as dry dust particles, but that the droplets themselves, with their contained or adherent organisms, are deposited. The *B mycoides*, which is larger than *B. prodigiosus*, was conveyed through much shorter distances and remained in suspension a much shorter time. In coughing and sneezing, more droplets are expelled than in speaking, and they are thrown to a greater distance, because of the greater amount of force employed.

The danger of infection through droplets can be prevented in great part by holding the hand or a handkerchief before the mouth while sneezing or coughing. Speaking should be restricted as much as possible, and in especially serious conditions the use of gauze veils before the mouth may be advised. Thus the air itself and all objects in the vicinity of the patient will be protected from infection. The precautions mentioned apply not alone to tuberculosis, but to diphtheria, whooping-cough, and other diseases, the organisms of which are found in the air-passages.

The Toxin of the Colon Bacillus.—Since the discovery by PROFESSOR V. C. VAUGHAN and MCCLYMONDS that practically all samples of American cheese contain the colon bacillus and that cultures of this organism may be boiled without destroying its toxicity, work on its toxin has been carried further by the former (*American Medicine*, May 18, 1901, p. 302), assisted by Cooley and Gelston. The bacilli with which they worked were obtained from cheese, water, and normal feces, and their virulence was intensified by passage through a number of animals. After inoculation of Roux flasks of 2 per cent. agar with a beef-tea culture of the bacillus and subsequent incubation, the growths were scraped from the surface of the agar and used in the preparation of the toxin. The facts learned from numerous experiments with the germ substance thus obtained are summed up as follows: The toxin is contained within the germ-cell, from which it does not, at least under ordinary conditions, diffuse into the culture medium. It is not extracted from the cell by alcohol, ether, or very dilute alkalies, nor is it destroyed when the germ-substance is heated to a high temperature with water. Neither the germ-cell nor its toxin is much, if at all, affected by boiling with a 2 per cent. solution of hydrochloric acid, but the former is broken up and the latter affected, but not destroyed, by being heated for an hour on the water-bath with water containing from 1 to 5 per cent. of the acid, and the toxin is made inert by prolonged heating. The toxin, separated from the cell wall by digestion of the latter with 2 per cent. hydro-

chloric acid and 0.5 per cent. pepsin, is markedly active and stable, and can be permanently preserved in the dry state.

How the toxin, if confined in the cell wall, is set free when the living or dead germ is introduced into an animal; whether, if this is accomplished by phagocytic action, the phagocytes destroy the toxin when they kill the germ; whether the cell contains both a toxin and an immunizing body, or the toxin can be converted by artificial means or within the system into an immunizing body, are questions under investigation.

Hydrocyanic Acid Gas as a Disinfectant.—In a preliminary note on the disinfectant properties of hydrocyanic gas, DR. J. S. FULTON (*American Medicine*, May 11, 1901, p. 256) gives the results of a number of experiments and suggests this agent as a reliable germicide for the disinfection of houses and ships. With regard to the feeling of danger which its employment in public health work might excite, attention is called to the extensive use of potassium cyanide in the industrial arts and of the gas in the disinfection of nursery stock and green-houses, with practically no record of accidents. Against organisms no hardier than those of diphtheria and typhoid fever it appears to be about as effective as formaldehyde, though more gas is needed and perhaps a longer exposure. Like other gaseous agents, it possesses no marked power of penetration. In the experiments iron wire, wet, was attacked by the gas and received a thin coat of Prussian blue; paper labels were stained brown; and cotton, exposed several times, became brown and brittle. The gas is best generated by the action of dilute sulphuric acid (acid 1.5 part, water 2.25 parts) on potassium cyanide (1 part), the contact taking place in earthen jars. About 1 kilogramme of cyanide is required for each 1000 cubic feet of air space. The poisonous properties of the gas make it necessary to exercise caution in its use and to ventilate well on the expiration of the period of exposure.

[In view of the greater cost of material for the disinfection of a given place, the possible danger attending its use, and the admitted inferiority to formaldehyde as a general germicide, it would appear that the only advantage attending its use is its superior toxicity to animal life, on which account, as the author points out, it has been extensively used in flouring-mills (weevils), railway cars (bed-bugs), tobacco warehouses (insects in general), and might be very useful for killing rats and other vermin in ships' holds.—C. H.]

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OF THE MEDICAL SCIENCES.

OCTOBER 19, 1901.

OFFICIAL REPORT OF THE CASE OF

PRESIDENT WILLIAM McKINLEY

BY THE MEDICAL ATTENDANTS.

THE following report has received the approval of and is issued by the undersigned, the medical staff attending the late President William McKinley.

P. M. RIXEY, EUGENE WASDIN,
MATTHEW D. MANN, CHARLES McBURNEY,
HERMAN MYNTER, CHARLES G. STOCKTON.
ROSWELL PARK,

SURGICAL HISTORY.

PRESIDENT WILLIAM McKINLEY was shot by Leon F. Czolgosz in the Temple of Music, at the Pan-American Exposition, Buffalo, N. Y., at about seven minutes past 4 on the afternoon of Friday, September 6, 1901. Two shots were fired. One bullet struck near the upper part of the sternum, and the other in the left hypochondriac region. The President was immediately conveyed to the Emergency Hospital on the Exposition grounds by the motor ambulance, where he arrived at 4.18. Dr. G. McK. Hall and Mr. Edward C. Mann, medical student of the house staff, were in charge of the ambulance, Medical Student T. F. Ellis being the driver.

On arriving at the hospital President McKinley was at once placed upon the table in the operating-room and undressed. During the removal of his clothing a bullet fell out and was picked up by Mr. Ellis. Dr. Hall placed a temporary antiseptic dressing over the wounds, and Mr. Mann ordered a nurse to administer 0.01 gramme of morphine and 0.002 gramme of strychnine hypodermically.

Dr. Herman Mynter, who had been telephoned from police headquarters to report immediately at the Exposition Hospital, was the first surgeon to arrive, at 4.45 o'clock. At that time Drs. P. W. Van Peyma and Joseph Fowler, of Buffalo, N. Y., and Dr. Edward Wallace Lee,

of St. Louis, were present. Dr. Mynter brought with him Dr. Eugene Wasdin, of the United States Marine Hospital Service.

Dr. Mynter inspected the President's wounds and immediately saw their serious nature. He told the President that it would be necessary to operate, and at once set about making preparations, aided by the house staff and nurses and Dr. Nelson W. Wilson, Sanitary Officer of the Exposition, who at that time assumed charge of the hospital in the absence of Dr. Roswell Park, the Medical Director of the Exposition. The President's pulse on the arrival of Dr. Mynter was 84; he had no particular pain in the abdomen, and no apparent loss of liver dulness. He was evidently slightly under the influence of the morphine.

Dr. Matthew D. Mann arrived at the hospital at 5.10 P.M., having been telephoned for by Mr. John C. Milburn. He was followed five minutes later by Dr. John Parmenter.

An examination was at once made, followed by a short consultation between Drs. Mann, Mynter, and Wasdin, which resulted in the decision to operate at once. The necessity for the operation was explained to President McKinley, and he gave his full consent. Immediate operation was decided upon because of the danger of possible continued internal hemorrhage and of the escape of gastric or intestinal contents into the peritoneal cavity, and because the President's pulse was getting weaker. Moreover, the daylight was rapidly failing. Dr. Roswell Park, who, by virtue of his office, had he been present would have performed the operation, was at Niagara Falls, and although a special train had been sent for him, it was uncertain when he would arrive.

Dr. Mann was selected to do the operation, with Dr. Mynter as his associate, by the common consent of the physicians present, and at the request of Mr. Milburn, President of the Pan-American Exposition, who stated that he had been requested by President McKinley to select his medical attendants. Dr. Mann selected Drs. Lee and Parmenter as assistants.

At 5.20 Dr. Mann directed the administration of ether to President McKinley, and requested Dr. Wasdin to administer it. Ether was chosen as being, on the whole, the safer anæsthetic. While the anæsthetic was being given the surgeons who were to take part in the operation prepared their hands and arms by thoroughly scrubbing with soap and water and immersing them in a solution of bichloride of mercury.

The operation began at 5.29. Dr. Mann stood upon the right-hand side of the patient, with Dr. Parmenter on his right-hand side. Dr. Mynter stood upon the left-hand side of the patient, and on his right was Dr. Lee. To Drs. Parmenter and Lee were assigned the duties of sponging and the care of the instruments. Dr. P. M. Rixey, U.S.N., President McKinley's family physician, having been detailed by the President to accompany Mrs. McKinley to the Milburn home, did not arrive until 5.30, when he gave very efficient service by guiding the

rays of the sun to the seat of the operation by aid of a hand-mirror, and later by arranging an electric light. Dr. Roswell Park arrived just as the operation on the stomach was completed, and gave his aid as consultant. Mr. E. C. Mann had charge of the needles, sutures, and ligatures. Mr. Simpson, medical student, was at the instrument tray.

The nurses, under the charge of Miss A. C. Walters, superintendent of the hospital, were Miss M. E. Morris and Miss A. D. Barnes, with hands sterilized; Miss Rose Baron, Miss M. A. Shannon, and Miss L. C. Dorchester, assistants, and Miss Katharine R. Simmons attending the anæsthetizer.

Beside those immediately engaged in the operation there were present Drs. P. W. Van Peyma, Joseph Fowler, D. W. Harrington, and Charles G. Stockton, of Buffalo, and Dr. W. D. Storer, of Chicago.

The Operation.

President McKinley took the ether well, and was entirely under its influence in nine minutes after the beginning of the anæsthetization. The abdomen was carefully shaved and scrubbed with green soap, and then washed with alcohol and ether and the bichloride solution.

Inspection showed two wounds made by the bullets. The upper one was between the second and third ribs, a little to the right of the sternum. The use of a probe showed that the skin had not been penetrated, but that the bullet had probably struck a button or some object in the clothing which had deflected it. The lower wound made by the other bullet—a thirty-two calibre—was on a line drawn from the nipple to the umbilicus. It was about half-way between these points and about 5 cm. to the left of the median line. A probe showed that this wound extended deeply into the abdominal walls, and that the direction was somewhat downward and outward.

An incision was made from the edge of the ribs downward, passing through the bullet wound and nearly parallel with the long axis of the body. A deep layer of fat was opened, and followed by incision of the fascia and muscles to the peritoneum. After cutting through the skin, a piece of cloth, undoubtedly a bit of the President's clothing, was removed from the track of the bullet, a short distance below the skin.

On opening the peritoneum the finger was introduced and the anterior wall of the stomach palpated. An opening was discovered which would not quite admit the index finger. This opening was located near the greater curvature of the stomach and about 2 cm. from the attachment of the omentum; its edges were clean-cut and did not appear to be much injured.

The stomach was drawn up into the operation wound, and the perforation very slightly enlarged. The finger was then introduced and the contents of the stomach palpated. This was done to see if the

stomach contained food, and also with the hope that possibly the bullet might be in the stomach. The stomach was found to be half-full of liquid food, but no evidence of the ball was discovered. In pulling up the stomach a small amount of liquid contents escaped, together with a good deal of gas. The tissues around the wound were carefully irrigated with hot salt solution and dried with gauze pads. The perforation in the anterior stomach wall was then closed with a double row of silk sutures (Czerny-Lembert). The sutures were not interrupted with each stitch, but four stitches were introduced before the ends were tied. The loop was then cut off and the sutures continued. About eight stitches were used in each row. The silk used was fine black silk, the needle being a straight, round sewing needle.

In order to examine the posterior wall of the stomach it was necessary to enlarge the incision, which now reached about 15 cm. in length. The omentum and transverse colon were pulled well out of the abdomen. The omentum was enormously thickened with fat and very rigid. In order to reach the back wall of the stomach it was necessary to divide about four inches of the gastrocolic omentum, the cut ends being tied with strong black silk in two masses on each side. In this way the stomach could be drawn up in the operation wound and the bullet wound in its posterior wall reached. This opening was somewhat larger than that in the anterior wall of the stomach, and had frayed and blood-infiltrated edges. Its exact location was impossible to determine, but it appeared to be near the larger curvature.

This opening was closed in the same way as the anterior wound, but with great difficulty, as the opening was down at the bottom of a deep pocket. A short curved surgical needle was necessary here. Little or no gastric contents appeared around this opening, but after it had been closed the parts were carefully irrigated with hot salt solution.

The operation on the stomach being now finished, Dr. Mann introduced his arm so as to palpate carefully all the deep structures behind the stomach. No trace of the bullet or of the further track of the bullet could be found. As the introduction of the hand in this way seemed to have a bad influence on the President's pulse, prolonged search for further injury done by the bullet, or for the bullet itself, was desisted from. The folds of the intestine which had been below the stomach were inspected for injury, but none was found. The entire gut was not removed from the abdomen for inspection, as the location of the wound seemed to exclude its injury. To have made a satisfactory search for wounds in the President's back it would have been necessary to have entirely eviscerated him. As he was already suffering from shock, this was not considered justifiable, and might have caused his death on the operating-table.

Before closing the abdominal wound Dr. Mann asked each of the surgeons present whether he was entirely satisfied that everything had

been done which should be done, and whether he had any further suggestions to make. Each replied that he was satisfied. The question of drainage was also discussed. Dr. Mynter was in favor of a Mikulicz drain being placed down behind the stomach wall. Dr. Mann, with the concurrence of the other surgeons, decided against this, as being unnecessary.

As the last step in the operation the tissues around the bullet track in the abdominal wall were trimmed in order to remove any tissue which might be infected. The abdominal wound was then closed with seven through-and-through silkworm-gut sutures, drawn only moderately tight, the superior layer of the fascia of the rectus muscle being joined with buried catgut. The edges of the skin were brought together by fine catgut sutures. Where the bullet had entered there was slight gaping of the tissues, but it was not thought advisable to close this tightly, as it might allow of some drainage. The wound was then washed with hydrogen dioxide and covered with aristol powder and dressed with sterilized gauze and cotton, which were held in place with adhesive straps. Over all was put an abdominal bandage.

The President bore the operation very well. The time from the beginning of the administration of the anæsthetic until its discontinuance was exactly an hour and thirty-one minutes; the operation was completed at 6.50 P.M., having lasted from the time of the first incision an hour and twenty-one minutes. At the beginning of the operation President McKinley's pulse was 84. At 5.38, 0.002 gramme of strychnine was administered hypodermically. At 5.55 the respiration was 32 and the pulse 84—both good in character. At 6.09 the pulse was 88. At 6.20 it was 102, fair in character; respiration 39. At 6.22, 1.50 gramme of brandy was administered hypodermically. At 6.48 the pulse was 124, the tension good but quick; respiration 36. At 7.01, after the bandage was applied, the pulse was 122 and the respiration 32. At 7.17, 0.004 gramme of morphine was administered hypodermically.

At 7.32 the patient was removed from the hospital in the ambulance. Dr. Rixey asked Drs. Park and Wasdin to go in the ambulance, as his duty called him to go at once to inform Mrs. McKinley of her husband's condition and to prepare a room for his reception. Drs. Mann and Mynter, with friends of the President, followed in carriages immediately after. President McKinley had not then recovered from the anæsthetic. He bore the journey to Mr. Milburn's house exceedingly well, but it was found necessary to give him a small hypodermic injection of morphine during the transit, as he was becoming very restless. On arrival at the house of Mr. Milburn, 1168 Delaware Avenue, he was removed from the ambulance on the stretcher, and carried to a room in the northwest corner of the house, where a hospital bed had been prepared for him.

REMARKS ON THE OPERATION. BY MATTHEW D. MANN, M.D.

The difficulties of the operation were very great, owing partly to the want of retractors and to the failing light. The setting sun shone directly into the room, but not into the wound. The windows were low and covered with awnings. After Dr. Rixey aided us with a hand-mirror the light was better. Toward the end of the time a movable electric light with reflector was put in use. The greatest difficulty was the great size of President McKinley's abdomen and the amount of fat present. This necessitated working at the bottom of a deep hole, especially when suturing the posterior wall of the stomach.

The operation was rendered possible and greatly facilitated by a good operating-table and the other appliances of a hospital and by the presence of many trained nurses and assistants. Still, the hospital was only equipped for minor emergency work, and had but a moderate supply of instruments. Unfortunately, when called I was not told what I was wanted for, and went to the Exposition grounds entirely unprepared. Dr. Mynter had his large pocket case, the contents of which were of great use.

As has already been noted, further search for the bullet was rendered inadvisable by the President's condition. The autopsy shows that it could not have been found, and that the injuries inflicted by the bullet after it passed through the stomach were of such a nature as to render impossible and unnecessary any further surgical procedure. A bullet after it ceases to move does little harm. We were often asked why after the operation we did not use the X-ray to find the bullet. There were several reasons for this. In the first place, there were at no time any signs that the bullet was doing harm. To have used the X-ray simply to have satisfied our curiosity would not have been warrantable, as it would have greatly disturbed and annoyed the patient, and would have subjected him also to a certain risk. Had there been signs of abscess formation, then the rays could and would have been used.

My reason for not draining was that there was nothing to drain. There had been no bleeding nor oozing; there was nothing to make any discharge or secretion; the parts were presumably free from infection, and were carefully washed with salt solution. As there was no peritonitis and the abdomen was found post-mortem to be sterile, we may safely conclude that no drainage could have been provided which would have accomplished anything. My experience teaches me never to drain unless there is a very decided indication for it, as a drain may do harm as well as good.

In conclusion, I wish to thank all the gentlemen who so kindly and skilfully assisted me. They were all surgeons of large experience in abdominal surgery, and their aid and advice were most valuable. Especially I wish to acknowledge my great obligation to my associate,

Dr. Mynter. Not only was he an assistant, but he was much more, and helped me greatly by his skill, and, as a consultant, with his good judgment and extensive knowledge of abdominal work. Although called first, he waived his claim and generously placed the case in my hands, willingly assuming his share of the responsibility.

The anæsthetic was most carefully administered by Dr. Wasdin, and the knowledge that he had charge of this very important duty relieved me of any anxiety on that score.

In the eventful week that followed the operation, Dr. Park and Dr. McBurney were towers of strength in helping to decide the many difficult questions which came up.

Dr. Rixey was in constant charge of the sick-room, aided later by Dr. Wasdin, who was detailed for this special duty. Both were unremitting in their care, and faithful to the end.

Dr. Stockton helped us in the last three days with the highest skill and best judgment.

Never, I am sure, under like circumstances, was there a more harmonious or better-agreed band of consultants. That our best endeavors failed was, I believe, no fault of ours; but it must be an ever-living and keen regret to each one of us that we were not allowed the privilege of saving so noble a man, so attractive a patient, and so useful a life.

The After Treatment.

When put to bed the President was in a fair condition: Pulse, 127; temperature, 100.6°; respiration, 30. The nurses on duty were Miss K. R. Simmons and Miss A. D. Barnes, from the Emergency Hospital. Soon after his arrival, at 8.25, he was given morphine, 0.016 gramme, hypodermically. There was slight nausea. The pulse soon improved. During the evening the patient slept at intervals, vomiting occasionally, but rallied satisfactorily. A slight discoloration of the dressings was noted at 10.45. There was occasional and slight pain. Ninety c.c. of urine was voided, and an enema of salt solution given and retained.

Second day, Saturday, September 7. After midnight the patient slept a good deal; he was free from pain and quite comfortable.

At 6 A.M the temperature was 102°; pulse, 110; respiration, 24.

Gas in large quantities was expelled from the bowels. A saline enema was given as before. Miss Simmons and Miss Barnes were replaced by Miss Maud Mohan and Miss Jane Connolly. Miss E. Hunt, of San Francisco, Cal., Mrs. McKinley's nurse, also rendered assistance, and Miss Grace Mackenzie, of Baltimore, Md., arrived September 9th, and was detailed for regular duty. P. A. Eliot, J. Hodgins, and Ernest Vollmeyer, of the United States Army Hospital Corps, were detailed as orderlies.

During the forenoon 0.01 gramme of morphine was administered hypodermically.

At 1.15 P.M. a saline enema of 500 c.c. was given. As the pulse was rising, 0.06 gramme of fluid extract of digitalis was injected hypodermically.

The President rested quietly until 6.30 P.M., when he complained of intense pain in the pit of the stomach, and was given 0.008 gramme of morphine sulphate hypodermically. He was very restless, but after being sponged rested again.

At 6.30 P.M. the pulse was 130; temperature, 102.5°; respiration, 29.

During the day the digitalis and morphine, and the saline enemas were kept up at regular intervals; 4 grammes of somatose were added to the water at 10.30 P.M. At 11.15 P.M. the President passed from the bowels 240 c.c. of a greenish-colored fluid and some particles of fecal matter.

The total amount of urine for twenty-four hours was 270 c.c.

First Urinalysis, by Dr. H. G. Matzinger.

Quantity	30. c.c.
Color	dark amber.
Reaction	strongly acid.
Urea	0.026 gm. per 1 c c. of urine.
Albumin	a trace.
Phosphates and chlorides	normal.
Sugar	none.
Indican	very small amount.

Microscopical Examination. The sediment obtained by centrifuge shows a large amount of large and small epithelial cells, with some leucocytes and occasional red cells. There is a comparatively large number of hyaline casts, principally small, with some finely granular ones; also an occasional fibrinous one. The amount of sediment is large for the quantity of urine submitted. There were no crystals in the sediment.

Third day, Sunday, September 8th. During the early morning the President slept a good deal, but was restless, and at times confused and a little chilly. On the whole, he passed a fairly good night.

He expelled a little gas and brown fluid from the rectum. The digitalis was continued, and at 7.45 A.M. 0.002 gramme of strychnine was given hypodermically. At 8.20 A.M. he was clear and bright, with the pulse strong and of good character.

The wound was dressed at 8.30, and found in a very satisfactory condition. There was no indication of peritonitis. Pulse, 132; temperature, 102.8°; respiration, 24.

The dressing on the wound was changed because there was some exudation. The bullet tract was syringed out with hydrogen dioxide. There was very little foaming, and there were no signs of pus.

At 10.40 A.M., following an enema of Epsom salts, glycerin, and water, he had a small stool with gas, and another at noon. He was less restless and slept a good deal.

At noon Dr. Charles McBurney, having been summoned by Dr. Rixey, joined the medical staff in consultation.

Bulletin 14, 12 M. The improvement in the President's condition has continued since the last bulletin. Pulse, 128; temperature, 101°; respiration, 27.

During the day he continued to improve; he slept four or five hours, and his condition was satisfactory.

At 4.45 P.M. he was given a teaspoonful of water by the mouth; also an enema of sweet oil, soap, and water. He passed slightly colored fluid with some little fecal matter and mucus. After this he had a small quantity of water by the mouth, and at 6.20 P.M. a nutritive enema of egg, whiskey, and water, which was partly retained. Digitalis and strychnine were both given during the evening.

At 9.P.M. the President was resting comfortably. The pulse was 130; temperature, 101.6°; respiration, 30.

Four hundred and twenty c.c. of urine was passed during the day.

Second Urinalysis.

Quantity	450 c.c.
Color	amber, slightly turbid.
Reaction	strongly acid.
Specific gravity	1.026.
Urea	0.038 gm. per 1 c.c. of urine.
Albumin	mere trace.
Sugar	none.
Indican	abundant.
Sulphates	increased.
Phosphates and chlorides	somewhat increased.

Microscopical Examination. Microscopical examination of sediment obtained by centrifuge shows fewer organic elements. Some large and small epithelial cells and some leucocytes. Casts are not so abundant as yesterday, and are principally of the small finely granular variety. There is a marked diminution in the small renal epithelial cells.

Quite a quantity of large crystals of uric acid and bacteria are present.

Fourth day, Monday, September 9. The bulletins tell the story of the fourth day.

Bulletin 17, 6 A.M. The President passed a somewhat restless night, sleeping fairly well. General conditions remained unchanged. Pulse, 120; temperature, 101°; respiration, 28.

Bulletin 18, 9.20 A.M. The President's condition is becoming more and more satisfactory. Untoward incidents are less likely to occur. Pulse, 122; temperature, 100.8°; respiration, 28.

Bulletin 19, 3 P.M. The President's condition steadily improves, and he is comfortable, without pain or unfavorable symptoms. Bowel and kidney functions normally performed. Pulse, 113; temperature, 101°; respiration, 26.

Bulletin 20, 9.30 P.M. The President's condition continues favorable. Pulse, 112; temperature, 101°; respiration, 27.

Codeia was substituted for morphine, as the pain was less. Digitalis and strychnine were stopped. Nutritive enemas were given at 3.20 A.M., 4.30 and 10 P.M. Hot water was taken quite freely by the mouth.

Attempts to get a good movement of the bowels were successful at noon, when he had a large light-brown, partly-formed stool. This followed a small dose of calomel and a high enema of oxgall.

On the whole the President's condition improved steadily during the day. He slept a good deal and was fairly comfortable. There was no pain on pressure over the abdomen.

Third Urinalysis.

Quantity received	540 c. c.
Color	amber, slightly turbid.
Specific gravity	1.026.
Albumin	a trace.
Indican	not so abundant as yesterday.
Urea	0.047 gm. per 1 c. c. of urine.
Chlorides and phosphates	about normal.
Sulphates	still somewhat high.
Sugar	none.

Microscopical Examination. Microscopical examination of sediment obtained by centrifuge shows a decrease in the amount of organic elements and an increase of amorphous urates, but fewer crystals of uric acid. Casts are fewer and only the small granular and large hyaline varieties. The proportion of casts is greater. There are very few epithelial cells, mostly of renal type. A large number of cylindroids are found.

Fifth day, Tuesday, September 10. Soon after midnight the President had a high enema of soap and water, which was expelled, together with some fecal matter. He took hot water frequently and slept a good deal.

Bulletin 21, 5.20 A.M. The President has passed the most comfortable night since the attempt on his life. Pulse, 118; temperature, 100.4°; respiration, 28.

On awaking he felt very comfortable, and his mind was clear and cheerful. The nutritive enemas were kept up and water given by the mouth. Had two small stools during the day. The only medicine given was one hypodermic of codeia phosphate, 0.015 gramme.

In the evening the dressings were examined, and as there was considerable staining from the discharge it was thought best to remove four stitches and separate the edges of the wound. A little slough was observed near the bullet track, covering a space nearly an inch wide, the thickness of the flaps. The separation seemed to extend down to the muscle. The surfaces, except those mentioned, looked healthy, but not granulating. It was supposed that the infection of the wound occurred either from the bullet or from the piece of clothing carried into the wound at the time of the shooting. The parts were thoroughly washed with hydrogen dioxide and packed lightly with gauze, and held together with adhesive straps.

Sixth day, Wednesday, September 11.—*Bulletin* 26, 9 A.M. The President rested comfortably during the night. Decided benefit has followed the dressing of the wound made last night. His stomach tolerates the beef juice well, and it is taken with great satisfaction. His condition this morning is excellent. Pulse, 116; temperature, 100.2°.

Bulletin 27, 3.30 P.M. The President continues to gain, and the wound is becoming more healthy. The nourishment taken into the stomach is being gradually increased. Pulse, 120; temperature, 100.2°.

Bulletin 28, 10 P.M. The President's condition continues favorable. Blood count corroborates clinical evidence of the absence of any blood poisoning. He is able to take more nourishment and relish it. Pulse, 120; temperature, 100.4°.

The blood count made by Dr. Wasdin in the evening was as follows:

Leucocytes	6,752
Red cells	3,920,000

A little after midnight Wednesday morning the patient was given 4 c. c. of beef juice, the first food taken by the stomach. It seemed to be very acceptable. Nutritive enema was given at 2 A.M.; later there was a yellow stool.

From 4 to 8 c. c. of beef juice was given every one to two hours during the day. The rectum was becoming irritable, and did not retain the nutritive enemas well.

At 10 A.M. the remaining stitches were removed, the wound separated and dressed. It seemed to be doing well. Most of the sloughing tissue had separated.

The patient slept much during the day, and expressed himself as feeling very comfortable. The only medicine administered was one hypodermic of strychnine.

In the evening he was changed to a fresh bed. Nutritive enemas were continued.

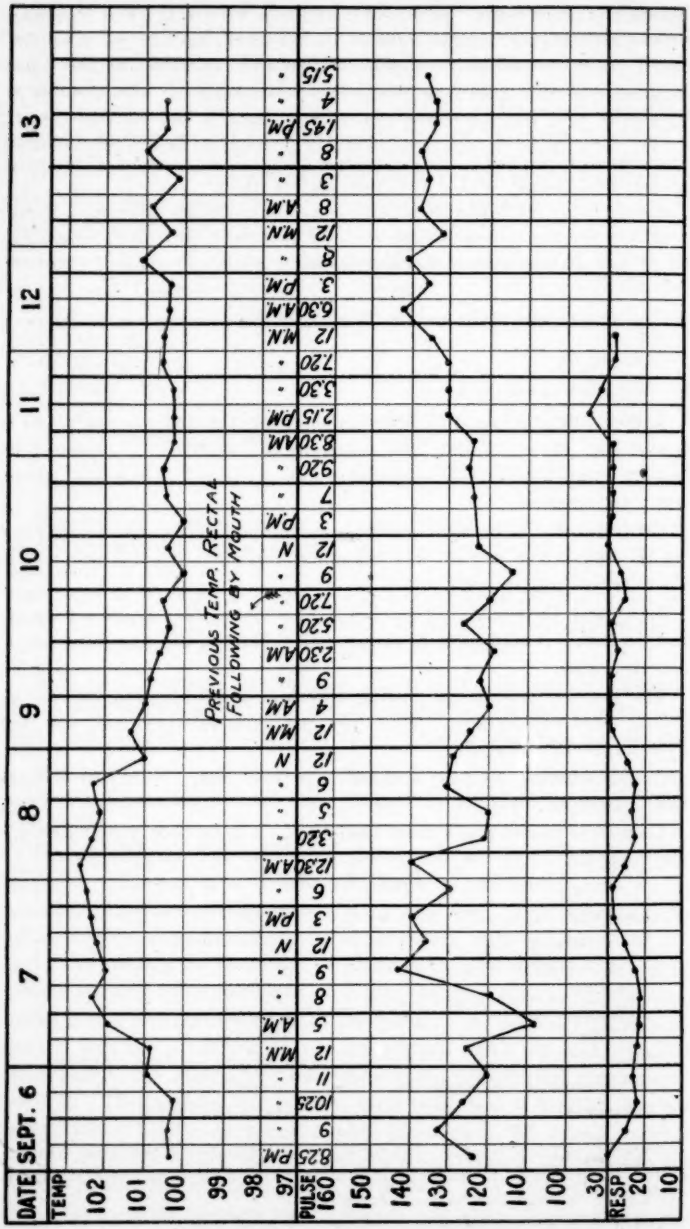
Urine was passed much more freely—750 c. c. in twenty-four hours.

Fourth Urinalysis.

Quantity	82 c.c.
Color	amber, clear.
Specific gravity	1.027.
Reaction	strongly acid.
Albumin	a trace.
Indican	abundant.
Urea	0.04 gm. per 1 c.c. of urine.
E. phosphates and chlorides	normal.
Sulphates	still a little high.

Microscopical Examination. Microscopical examination of sediment obtained by centrifuge shows a marked diminution in amount of organic elements, but a great increase in uric acid crystals.

There are a few epithelial cells—mostly of renal type.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PREVIOUS TEMP. RECTAL
FOLLOWING BY MOUTH

There are fewer casts—small and large hyaline—some finely granular. Cylindroids are more abundant.

Seventh day, Thursday, September 12th. The President slept a good deal during the night, and awoke in the morning feeling better. The beef juice was continued and increased, and a little chicken-broth added to the dietary. He also had a little whiskey and water.

At 8.30 A M. he had chicken-broth, a very small piece of toast and a small cup of coffee. He did not care for the toast, and ate scarcely any of it.

The wound was dressed and washed with a weak solution of iodine and then with hydrogen dioxide. He was given 30 c.c of castor oil at 9.20 A.M.

The President now seemed at his best and his condition to warrant the favorable prognosis given out. The time for peritonitis and sepsis had passed. The bowels had moved and gas passed freely, showing that there was no obstruction. The tongue was clear, and the appetite increasing; and he seemed to be able to digest food. There was no pain or tenderness in the abdomen, and he was able to turn easily and to sleep on his side. The urine was steadily increasing. His spirits were good and his mind clear, while his pulse, though frequent, was strong and of good quality, and the temperature low.

The analysis of the urine gave no uneasiness, as the amount of urea was fair; there was no albumin worth considering, and the casts were rapidly diminishing. There were no more of them than are found in a large percentage of cases following a long operation under ether. The excess of indican was taken to mean merely some intestinal indigestion, and to be of no serious import. The only symptom to cause any uneasiness was the frequency of the pulse. Still, anxiety on this score was relieved by knowing that the President had naturally a rapid pulse, and that it was easily excited. The open wound was not considered important. It looked healthy, and, though it would take a long time to heal, in itself it was evidently causing no harm, nor was it likely to.

Dr. McBurney left Buffalo for his home in the morning, having arranged to return at once if his presence was desired.

Toward noon it was noticed that the character of the pulse was not quite so good. Infusion of digitalis, 8 c.c., was ordered, and strychnine, 0.002 gramme.

It was thought probable that there was some intestinal toxæmia, as there had been no free movement from the bowel since food had been begun, the oil having failed to act. Gradually the pulse went to 130, and grew weaker.

Dr. Charles G. Stockton was added to the medical staff in consultation. At 7 P.M. the President was given 0.20 gramme of calomel.

Bulletin 32, 8.30 P.M. The President's condition this evening is not quite so good. His food has not agreed with him, and has been stopped. Excre-

tion has not yet been properly established. The kidneys are acting well. His pulse is not satisfactory, but has improved in the last two hours. The wound is doing well. He is resting quietly. Temperature, 100.2°; pulse, 128.

At 9.30 P.M. a second dose of 30 c.c. of castor oil was given, followed by a high enema of oxgall. This resulted in a large, dark semi-fluid stool, which seemed to exhaust him somewhat. Stimulants were given freely. No more beef juice or food was given. The pulse grew rapidly worse, but at midnight there seemed some improvement, as Bulletin 33 shows. At 11 P.M. 420 c.c. of normal salt solution were given subcutaneously.

Bulletin 33, 12 M. All unfavorable symptoms in the President's condition have improved since the last bulletin. Pulse, 120; temperature, 100.2°.

Fifth Urinalysis.

Quantity	132 c.c.
Color	light amber, very turbid.
Specific gravity	1.025.
Reaction	acid.
Albumin	mere trace, if any.
Indican	less.
Urea	0.044 gm. per 1 c.c. of urine.
Sulphates	about normal.
E. phosphates	much increased.
Chlorides	normal.

Microscopical Examination. Microscopical examination of sediment obtained by centrifuge shows fewer organic elements than the last examination. There is less uric acid and a large amount of amorphous phosphates. Renal casts, about as in the last examination, with very few cylindroids.

Eighth day, Friday, September 13. At midnight the pulse was fairly good, 132. Strychnine and whiskey were given at intervals, and hypodermics of camphorated oil.

Bulletin 34, 2.50 A.M. The President's condition is very serious, and gives rise to the gravest apprehension. His bowels have moved well, but his heart does not respond properly to stimulation. He is conscious. The skin is warm, and the pulse small, regular, easily compressible, 126; respiration, 30; temperature, 100°.

The wound had been dressed regularly in the manner described three times a day. At 9 A.M. the dressing was changed, and a mixture of balsam of Peru and glycerin put in on gauze after the douching.

Stimulants were continued as before, but more freely. Coffee, 45 c.c., and clam-broth, 60 c.c., were given; also, liquid peptonoids.

At 8.30 A.M. 1.50 gramme of adrenalin was given hypodermically, and repeated at 9.40.

At 10 A.M. nearly two pints of normal salt solution were given under the skin, and a pint, containing adrenalin, at 6 P.M. Nitroglycerin and

camphor were also injected at various times, together with brandy and strychnine.

Stimulants, as detailed above, were used freely all day.

3.30 P.M. Pulse growing weaker.

5 P.M. Oxygen given, and continued for some hours.

6.30 P.M. Last bulletin, No. 39:

Bulletin 39, 6.30 P.M. The President's physicians report that his condition is most serious in spite of vigorous stimulation. The depression continues, and is profound. Unless it can be relieved the end is only a question of time.

At 6.35 P.M., and again at 7.40, morphine was given hypodermically, as he was very restless and seemed to be suffering.

9 P.M. Heart-sounds very feeble.

The President continued to sink, becoming weaker and weaker.

At 10 P.M. the oxygen was discontinued. The heart-sounds were very feeble and consciousness lost.

The President died at 2.15 A.M., September 14th.

Drs. E. J. Janeway and W. W. Johnston, who, at the request of Dr. Rixey, had been summoned in consultation, arrived too late, but were present at the autopsy. Dr. McBurney also returned on Friday afternoon.

Sixth Urinalysis.

Color	amber, turbid, with phosphates.
Quantity	252 c.c.
Reaction	acid.
Specific gravity	1.023.
Albumin	mere trace, if any.
Urea	0.047 gm. per 1 c.c. of urine.
Indican	a trace.
E. phosphates	increased.
Chlorides	normal.
Sulphates	a little high.

Microscopical Examination. Microscopical examination of sediment obtained by centrifuge, before and after clearing, shows no change from yesterday's sample. Casts, hyaline and granular, both large and small, comparatively few. Cylindroids, a few. Crystals, large amount of uric acid, some sodium urate, and in the untreated specimen a large amount of amorphous deposit, principally of phosphates. There are a few epithelial cells, small, granular. Occasional red cells and leucocytes.

REPORT ON THE AUTOPSY.[1] BY HARVEY R. GAYLORD, M.D.,

Pathologist to the New York State Pathological Laboratory.

Ordinary signs of death: Ecchymosis in dependent portions of the body. Rigor mortis well marked. Upon the surface of the chest, to the right of the midsternal line, a spot 1 cm. in diameter, dark red in color, with a slight

[1] The autopsy was performed by Drs. Gaylord and Matzinger.

crust formation covering it, 5.5 cm. from the suprasternal notch; from the right nipple, 10 cm.; from the line of the right nipple, 8.25 cm. Surrounding this spot, at which point there is an evident dissolution of the continuity of the skin, is a discolored area of oval shape extending upward and to the right. In its greatest length it is 11 cm., and in its greatest width 6 cm. It extends upward in the direction of the right shoulder. The skin within this area is discolored, greenish-yellow, and mottled.

The surface of the abdomen is covered with a surgical dressing, which extends down to the umbilicus and upward to just below the nipples. The innermost layer of cotton is covered or stained with balsam of Peru and blood. On removing this dressing, a wound, parallel to and somewhat to the left of the median line, is exposed, inserted in which are two layers of gauze, likewise impregnated with balsam of Peru. The wound is 14.5 cm. in length, and is open down to the abdominal muscles. The layer of abdominal fat is 3.75 cm. in thickness. The appearance of the fat is good, a bright yellow in color. No evidence of necrosis or sloughing. In the left margin of the surgical wound, lying 1 cm. to the right of a line drawn from the umbilicus to the left nipple, 15.5 cm. from the nipple and 16.5 cm. from the umbilicus, is a partly healed indentation of the skin, and an excavation of the fat immediately beneath it (this is the site of the entry of the bullet), extending down to the peritoneal surface. On making the median incision, starting from the suprasternal notch and extending to a point just below the symphysis, the subcutaneous fat is exposed, which is of bright yellow color and normal in appearance, except in an area which corresponds superficially to the area of discoloration described as surrounding the wound upon the chest wall. This area marks the site of a hemorrhage into the subcutaneous fat. The remainder of the subcutaneous fat is firm, and measures 4.75 cm. in thickness on the abdominal wall. On opening the sheath of the right rectus muscle it was seen to be of dark red color. (Culture taken from ecchymotic tissue under the upper bullet hole and from between the folds of the small intestine. Three tubes from each locality on agar and gelatin.)

On opening the abdominal cavity the parietal surface of the peritoneum is exposed, and is found to be covered with a slight amount of bloody fluid; is perfectly smooth and not injected. The great omentum extends downward to a point midway between the umbilicus and the symphysis. It is thick, firm; its inferior border is discolored by coming in contact with the intestines. Below the umbilicus a few folds of intestine are exposed. These are likewise covered with discolored blood, after the removal of which the peritoneal surface is found to be shiny. On the inner aspect of the abdominal wound the omentum is found to be slightly adherent to the parietal peritoneum, and can be readily separated with the hand from the edge of the wound. At this point the omentum is somewhat injected. This adhesion to the omentum is found to extend entirely around the abdominal wound. The parietal peritoneum immediately adjacent to the inner aspect of the abdominal wound is ecchymotic.

On removing the subcutaneous fat and muscles from the thoracic wall, the point which marks the dissolution of continuity of the skin upon the surface is found to lie directly over the margin of the sternum and to the right side between the second and third ribs. There is no evidence of ecchymosis or injury to the tissues or muscles beneath the subcutaneous fat. On making

an incision through the subcutaneous fat, directly through the wound upon the chest, a small cavity is exposed, about the size of a pea, just beneath the skin, which is filled with fluid blood. The subcutaneous tissue underlying the area of discoloration on the surface of the chest wall shows hemorrhagic infiltration.

On removing the sternum the lungs are exposed, and do not extend far forward. A large amount of pericardial fat is exposed. Pleural surface on both sides is smooth. There are no adhesions on either side within the pleural cavities. The diaphragm on the right side extends upward to a point opposite the third rib in the mammary line. No perceptible amount of fluid in either pleural cavity. On opening the pericardial cavity the surface of the pericardium is found to be smooth and pale. The pericardium contains approximately 6 c.c. of straw-colored, slightly turbid fluid. (Some taken for examination.)

On exposing the heart it is found covered with a well-developed panniculus. The heart measures, from the base to the apex on the superficial aspect, 10.5 cm. The right ventricle is apparently empty. The heart feels soft and flaccid. On opening the left ventricle a small amount of dark red blood is found. The muscle of the left ventricular wall is 1.5 cm. in thickness; dark reddish-brown in color; presents a shiny surface. The average thickness of the pericardial fat is 3.5 mm. (Cultures made from the auricle.) The left auricle contains but a small amount of dark, currant-colored blood. The mitral valve admits three fingers. The right ventricle, when incised in the anterior line, is found to be extremely soft; the muscular structure is 2 mm. in thickness. The panniculus measures 7 mm. The muscle is dark red in color, very shiny, and the pericardial fat invades the muscular wall at many points.

On opening the right auricle it is found to be filled and distended by a large currant-colored clot, which extends into the vessels. The tricuspid orifice admits readily three fingers. The coronary arteries are patulous and soft; no evidence of thickening.

Lungs are gray color, and contain a moderate amount of coal-dust pigment. Slight amount of frothy fluid escapes from the bronchi; but the pulmonary tissue is crepitant and free from exudate.

On unfolding the folds of intestine there is no evidence of adhesion until a point just beneath the mesocolon is reached, when, on removing a fold of small intestine, a few spoonfuls of greenish-gray, thick fluid flows into the peritoneal cavity.

On the anterior gastric wall is an area to which a fold of the gastrocolic omentum is lightly adherent. On breaking the adhesion there is found a wound about midway between the gastric orifices, 3.5 cm. in length, parallel with the greater curvature of the stomach, 1.5 cm. from the line of omental attachment. This wound is held intact by silk sutures. There is no evidence of adhesion at any other point on the anterior wall. The gastric wall surrounding the wound just mentioned for a distance of 2 cm. to 3 cm. is discolored, dark greenish-gray in appearance, and easily torn. On exposing the posterior wall of the stomach from above, along its greater curvature, the omentum is found to be slightly adherent, a line of silk ligatures along the greater curvature of the stomach marking the site where the omentum had been removed. On throwing the omentum downward the posterior

gastric wall is exposed. On the posterior wall, a distance of 2 cm. from the line of omental attachment, is a wound approximately 2 cm. long, held intact by silk sutures. The gastric wall surrounding this wound is discolored. On the surface of the mesocolon, which is posterior to the gastric wall at this point, is a corresponding area of discoloration, the portion coming directly in contact with the wound in the gastric wall being of dull gray color. The remainder of the surface of the posterior wall of the stomach is smooth and shiny. Beyond the surgical wound in the posterior wall of the stomach is found an opening in the retroperitoneal fat large enough to admit two fingers. This opening communicates with a track which extends downward and backward as far as the finger can reach. The tissues surrounding this track are necrotic. On removing the descending portion of the colon a large, irregular cavity is exposed, the walls of which are covered with gray, slimy material, and in which are found fragments of necrotic tissue. Just at the superior margin of the kidney is located a definite opening, which forms the bottom of the track traced from the stomach. On stripping the left kidney from its capsule it is found that the superior portion of the capsule is continuous with the cavity. The weight of the left kidney is 5 oz., 1 g. The kidney is readily stripped from its capsule; is dark red; the stellate veins are prominent, and along its greater curvature are numerous dark red depressions. On the superior aspect of the kidney is a protrusion of the cortex, dark red in color, and in this protrusion is a laceration, 2 cm. long, extending across the superior border, approximately at right angles to the periphery of the kidney and from before backward. On incising the kidney the cortex and medulla are not easily distinguishable from one another; both are of rose-red color, the cortex measuring approximately 6 mm. in thickness. The vessels in the pyramids of Ferrein are very prominent. Beneath the protruding portion of the surface the cortex is dark red in color. This discoloration extends downward in pyramidal form into the medulla. The laceration of the surface marks the apex of the protrusion of the kidney substance. Between the spleen and the superior aspect of the kidney is a necrotic tract which extends down and backward and ends in a blind pocket. The tract which included the superior aspect of the kidney can be traced into the perinephritic fat to a point just above the surface of the muscles of the back.

The necrotic cavity which connects the wound on the posterior wall of the stomach and the opening adjacent to the kidney capsule is walled off by the mesocolon, and is found to involve an area of the pancreas, approximately 45 mm. in diameter, and extending about half through the organ. This organ, at its centre, forms part of the necrotic cavity. Through its body are found numerous minute hemorrhages and areas of gray softening, the size of a pea or smaller. These are less frequent in the head portion of the pancreas.

A careful examination of the track leading down toward the dorsal muscles fails to reveal the presence of any foreign body. After passing into the fat the direct character of the track ceases, and its direction can be traced no further. The adjoining fat and the muscles of the back were carefully palpated and incised without disclosing a wound or the presence of a foreign body. The diaphragm was carefully dissected away, and the posterior portion of the thoracic wall likewise carefully examined. All fat and organs

which were removed, including the intestine, were likewise examined and palpated, without result.

The great amount of fat in the abdominal cavity and surrounding the kidney rendered the search extremely difficult.

The right kidney is embedded in a dense mass of fat; capsule strips freely; it weighs 5 ounces; measures 11.5 cm.; substance is soft; cortex is 6 mm. in thickness; rose-red in color; cut surface slightly dulled. There are a few depressions of the surface, and the stellate veins are prominent.

The liver is dark red in color; the gall-bladder distended. The organ was not removed.

The autopsy continued for a longer period than was anticipated by those who had charge of the President's body, and we were requested to desist seeking for the bullet, and terminate the autopsy. As we were satisfied that nothing could be gained by locating the bullet, which had apparently set up no reaction, search for it was discontinued.

Anatomical Diagnosis. Gunshot wound of both walls of the stomach and the superior aspect of the left kidney; extensive necrosis of the substance of the pancreas; necrosis of the gastric wall in the neighborhood of both wounds; fatty degeneration, infiltration, and brown atrophy of the heart muscle; slight cloudy swelling of the epithelium of the kidneys.

A matter of no inconsiderable embarrassment to us arose in the objection to our removing sufficient portions of the tissues for examination. We were able to secure only two small fragments of the stomach wall; tissue from around the wound upon the chest wall; a portion of fat from the wall of the necrotic cavity; a small piece of each kidney, that of the left kidney including the portion involved by the original wound; and pieces of heart muscle from the right and left ventricles. The microscopical examination of these tissues follows:

The piece of retroperitoneal fat, where it forms part of the necrotic cavity, is seen on section to be covered with a thick gray deposit, which has an average thickness of from 4 mm. to 6 mm. Beneath this, and separating it from the fat, is a well-defined area of hemorrhage, from 1 mm. to 2 mm. in thickness. The appearance of this piece of tissue is characteristic of the fat tissue surrounding the entire cavity. A section made perpendicular to the surface, and stained with hæmatoxylin-eosin, shows the following characteristics: Under low power there is no evidence of round-celled infiltration between the fat cells or of fat necroses. The surface of the tissue, which in the microscopical specimen was covered by a layer of grayish material, proves, under low power, to consist of a partly organized fibrinous deposit. At the base of this deposit is evidence of an extensive hemorrhage, marked by deposits of pigment. The surface of the membrane is of rough and irregular appearance, and contains a large number of round cells, with deeply stained nuclei. Under high power the organization of the membrane may be traced from the base toward the surface. The portion immediately adjacent to the fat tissue consists of a network of fibrin inclosing large numbers of partly preserved red blood-corpuscles. In many areas the red blood-corpuscles are broken down, and extensive deposits of pigment are found. Extending into the fibrin structure of the membrane are numerous typical fibroblasts and round cells. In some regions pigment is evidently deposited in the bodies of large branching and spindle cells. Here and there, included

in the membrane, are the remains of fat cells, and toward the surface of the membrane a large number of round cells scattered through the interstices of the membrane. There are but few polymorphonuclear leucocytes. Here and there in the membrane are fragments of isolated fibrous connective tissue, with irregular contours and an appearance suggesting that they are fragments of tissue which have been displaced by violence and included in the fibrin deposit. The fibrin in the superficial layers of the membrane is formed in hyaline clumps. The organization along the base of the deposit is comparatively uniform.

Sections stained with methylene blue, carbol-thionin, and Gram's method were carefully examined for the presence of bacteria, with negative results. Even upon the surface of the membrane there are no evidences of bacteria.

The section of the left kidney including the triangular area of hemorrhage described in the macroscopical specimen reveals the following appearances. (section hardened in formalin, stained with hæmatoxylin-eosin): Examined macroscopically, section represents a portion of a kidney cortex made perpendicular to the surface of the cortex, and including an area of hemorrhage into the substance of the cortex 1 cm. in length, measured from the capsular surface downward, and presenting a width of from 5 mm. to 6 mm. The capsular surface has apparently been torn.

Under low power the margins of the preparation are found to consist of well-preserved kidney structure. There is a slight amount of thickening of the interstitial tissue, and occasional groups of tubules are affected by beginning cloudy swelling. The glomeruli are large, and present a perfectly normal appearance. As we approach toward the centre of the preparation occasional glomeruli are met with in which the capillary loops are engorged, and the adjacent tubules contain red blood-corpuscles. A short distance further the kidney structure becomes entirely necrotic. Here and there the remains of tubules may be made out, and these are infiltrated with cells. The necrotic area presents a rough, net-like structure. As we approach toward the surface of the kidney we find that the necrosis becomes more marked. There is the merest suggestion of kidney structure, its place being taken by disintegrated red blood cells and leucocytes, embedded in a well-defined fibrinous network. There is great distortion of the kidney structure about the periphery of the necrotic area. In this region a considerable amount of pigment is also found in the necrotic tissues.

Under high power the characteristics of the necrotic tissues may be better observed. The kidney structure is broken up and torn into irregular fragments, infiltrated by red blood-corpuscles and leucocytes. In the portion of the necrotic mass beneath the capsule the kidney structure is practically obliterated and is replaced by a network of fibrin, which includes large numbers of red blood cells and leucocytes. Scattered through the entire necrotic area are frequent deposits of pigment. In the deeper portions of the necrotic area the margins of the fibrin deposit are invaded by fibroblasts from the connective tissue structure of the kidney. The organization in these areas is, however, slight.

Sections stained with methylene blue and Gram's method, and carefully examined under oil immersion, fail to reveal the presence of any organisms. In preparations stained with methylene blue the deposits of pigment may be readily observed. Section of the same tissue hardened in Hermann's solution and examined for fat shows the presence of numerous fat droplets within

the epithelium of the tubules which are adjacent to the area of necrosis. In the portions of the preparation more widely distant from the area of necrosis no fat is present.

Section of the right kidney hardened in formalin and stained with hæmatoxylin-eosin reveals the presence of areas in which slight parenchymatous degeneration of the epithelium in the uriniferous tubules may be noted. These areas are not extensive, and are confined to single groups of tubules. The interstitial connective tissue of the organ seems to be slightly increased in amount, but there is no well-defined round-celled infiltration. An occasional hyaline glomerulus is to be met with in these cases, surrounded by increased connective tissue. The epithelium of the kidney tubules, aside from those in which the parenchymatous degeneration is present, is well preserved. The nuclei are well stained; protoplasm finely granular.

A fragment of the stomach wall taken from the immediate neighborhood of the anterior wound is in a condition of complete necrosis. The nuclei of the cells are scarcely demonstrable. The epithelial surface is recognized with difficulty. At its base are apparently a few round cells. Examination of the bloodvessels reveals nothing characteristic. There is apparently no evidence of thrombosis A section made through the gastric wall at some distance from the wound reveals the well-preserved muscular structure of the gastric wall, which presents no characteristic alterations. Superficial portions of the epithelium have apparently been affected by post-mortem digestion. However, in one portion of the preparation the epithelium is intact, and shows distinct evidence of marked round-celled infiltration between the glandular structures. The bloodvessels contained blood-corpuscles, with the usual number of leucocytes.

The fragments of heart muscle which were removed from the right and left ventricular walls were examined in the fresh state, and exhibited a well-defined fatty degeneration of the muscle fibres, and in the case of the right ventricular wall an extensive infiltration between the muscle fibres of fat was apparent. Sections from these fragments of muscle hardened in Hermann's solution are taken for examination. A fragment of muscle from the right ventricular wall was removed at a point where the fat penetrated deeply into the muscular structure, the ventricular wall at this point showing an average thickness of 2.5 mm. Under low power the muscle fibres are separated into bundles by masses and rows of deeply stained fat cells. The muscle fibres are seen to contain groups of dark brown granules lying in the long axis of the cells. Under high power these are resolved into extensive groups of dark brown pigment arranged around the nuclei. The muscle fibres are slender, the cross and longitudinal striation is well-defined. Examined near the margin of the preparation, where the osmic acid fixation has been successful, all of the muscle fibres are found to contain minute black spherical bodies, extending diffusely through all the muscle fibres about the entire margin of the preparation. These fine fat droplets are present in sufficient amount to speak of an extensive diffuse fatty degeneration of the muscle fibres. Where the large fat cells have separated the muscle fibres these are found to be more atrophic than those in the central portions of the larger bundles.

The examination of the section through the healed bullet wound on the chest walls reveals nothing of importance. The dissolution of continuity is filled in by granulation tissue, and there is evidence of beginning restora-

tion of the epithelium from the margins. Stains for bacteria give negative results.

In summing up the macroscopical and microscopical findings of the autopsy the following may be stated: The original injuries to the stomach wall had been repaired by sutures, and this repair seems to have been effective. The stitches were in place, and the openings in the stomach wall effectually closed. Firm adhesions were formed both upon the anterior and posterior walls of the stomach, which reinforced these sutures. The necroses surrounding the wounds in the stomach do not seem to be the result of any well-defined cause. It is highly probable that they were practically terminal in their nature, and that the condition developed as a result of lowered vitality. In this connection there is no evidence to indicate that the removal of the omentum from the greater curvature and the close proximity of both of these wounds to this point had any effect in bringing about the necrosis of the gastric wall, although circulatory disturbances may have been a factor. The fact that the necrotic tissue had not been affected by digestion strongly indicates that the necrosis was developed but shortly before death. The excavation in the fat behind the stomach must be largely attributed to the action of the missile. This may have been the result of unusual rotation of a nearly spent ball, or the result of simple concussion from the ball passing into a mass of soft tissues. Such effects are not unknown. The fact that the ball grazed the superior aspect of the left kidney, shown by the microscopical investigation of that organ, indicates the direction of the missile, which passed in a line from the inferior border of the stomach to the tract in the fat immediately superior to the kidney. There was evidence that the left adrenal gland was injured.

The injury to the pancreas must be attributed to indirect, rather than direct, action of the missile. The fact that the wall of the cavity is lined by fibrin, well advanced in organization, indicates that the injury to the tissues was produced at the time of the shooting. The absence of bacteria from the tissues indicates that the wound was not infected at the time of the shooting, and that the closure of the posterior gastric wound was effectual. The necrosis of the pancreas seems to us of great importance. The fact that there were no fat necroses in the neighborhood of this organ indicates that there was no leakage of pancreatic fluid into the surrounding tissues. It is possible that there was a leakage of pancreatic fluid into the cavity behind the stomach, as the contents of this cavity consisted of a thick, grayish fluid, containing fragments of connective tissue. In this case the wall of fibrin would have been sufficient to prevent the pancreatic fluid from coming in contact with the adjacent fat. The extensive necrosis of the pancreas would seem to be an important factor in the cause of death, although it has never been definitely shown how much destruction of this organ is necessary to produce death. There are experiments upon animals upon record in which the animals seem to have died as a result of not very extensive

lesions of this organ. One experiment of this nature reported by Flexner (*Journal of Experimental Medicine*, vol. ii.) is of interest. The fact that concussion and slight injuries of the pancreas may be a factor in the development of necrosis is indicated by the researches of Chiari (*Zeitschrift für Heilkunde*, 1896, vol. xvii., and *Prager med. Wochenschr.*, 1900, No. 14), who has observed (although a comparatively rare condition) extensive areas of softening and necrosis of the pancreas, especially of the posterior central portion which lies directly over the bodies of the vertebra, where the organ is most exposed to pressure or the effects of concussion. The wound in the kidney is of slight importance, except as indicating the direction taken by the missile. The changes in the heart, as shown by the macroscopical inspection and the microscopical examination, indicate that the condition of this organ was an important factor. The extensive brown atrophy and diffuse fatty degeneration of the muscle, but especially the extent to which the pericardial fat had invaded the atrophic muscle fibres of the right ventricular wall, sufficiently explain the rapid pulse and lack of response of this organ to stimulation during life.

Report on the Bacteriological Examination. By Herman G. Matzinger, M.D.,

Bacteriologist to the New York State Pathological Laboratory.

It is obvious that the short space of time which has elapsed since the death of the President has hardly been sufficient to prepare a complete and thorough bacteriological report. This report contains all the observations which have been made up to this time.

On September 11th, during the life of the President, cultures were made by Dr. Wasdin from the base of the abdominal wound and from dressings removed at the same time. These were submitted to me for examination, and showed the presence of the ordinary pus organisms: Staphylococcus pyogenes aureus and staphylococcus cereus albus, with a gas-forming bacillus which, in pure anaërobic culture on glucose gelatin, forms small, pearly, translucent colonies, with no liquefaction. In litmus milk it produces acid, but no coagulation. Morphologically, it is apparently a capsulated, short bacillus, which takes stain poorly and which does not stain by Gram's method. Inoculated into the ear vein of a rabbit, which was killed immediately afterward, it produced, after twenty-four hours in the body of the rabbit, a marked accumulation of gas in the organs, and again grew out in pure culture. As yet the organism is not fully identified.

None of these cultures showed streptococci. A bacterium which appears to be one of the proteus group was, however, isolated, which does not stain by Gram and appears in varying forms, sometimes small, oval, and again quite rod-shaped and in short chains. Sometimes it is surrounded with a slimy covering, which remains clear like a capsule when the organism is stained. On slanting agar it produces a whitish, slimy growth, which gradually runs to the bottom of the slant and produces an odor of decomposition.

On gelatin it grows very slowly, with slight and slow indication of liquefaction. In litmus milk it produces acid and rapid coagulation.

At the time of the autopsy, September 14th, inoculations were made by myself. From the base of the wound there was again obtained a number of pus organisms, principally a white staphylococcus and the bacterium described above, but no streptococci. Cultures made from the peritoneal surface of the intestines were entirely negative. Cultures made from the under surface of the omentum, near the colon, were entirely negative, both with and without oxygen. Cultures from the blood of the right auricle were likewise negative. A very careful and extensive search for micro-organisms in the contents of the necrotic cavity behind the stomach reveals nothing but a short, stumpy bacterium, which, as far as the work has been carried at present, appears to belong to the proteus group, and is very like proteus hominis capsulatus, described by Bordoni and Uffreduzzi.

Morphologically, it is not uniform, and sometimes appears almost encapsulated, being surrounded by material that does not stain, is quite refractory to Gram, and produces an odor of decomposition as it grows. It does not liquefy gelatin rapidly, and grows slowly as a glistening, white elevated surface growth, which slowly sinks; but on agar, in the thermostat, it grows very rapidly as a moist, grayish-white, translucent mass. Colonies on gelatin plates have a clean circumference, are granular, and quite refractive. In litmus milk it produces acid and rapid coagulation. Animal experiments are still incomplete and cannot be published at this time.

It must be stated that there is occasion for suspecting that this may be a contamination, either from the outer wound or elsewhere, because, quite unavoidably, the technique of obtaining the material and cultures from the necrotic cavity was not absolutely correct.

Cultures made from the small area of broken-down tissue under the chest wound at the time of the autopsy grew what appears to be staphylococcus epidermidis albus described by Dr. Welch.

The slimy, gray necrotic material from the cavity above the transverse mesocolon behind the stomach was carefully examined microscopically, with the result that very few micro-organisms were found in the fresh state, and no recognizable tissue elements of any kind, no leucocytes or pus-corpuscles, but an abundance of crystals, which appeared more like fatty acid than fat crystals. It contained no free hydrochloric acid, and was alkaline in reaction. Experiments as to its digestive power were negative. About 2 c.c. of this material was injected in the space behind the stomach of a dog (still living), with no results except quite an elevated temperature for three or four days. Other animal experiments are also incomplete.

It might be well to state here that the bacteriological examination of the chambers and barrel of the weapon used, as well as the empty shells and cartridges, ordered by the District Attorney, was entirely negative, except that from a loaded cartridge there was grown an ordinary staphylococcus and a mould. The chemical examination of the balance of the loaded cartridges, made by Dr. Hill, chemist, was also negative.

The absence of known pathogenic bacteria, particularly in the necrotic cavity, warrants the conclusion that bacterial infection was not a factor in the production of the conditions found at the autopsy.

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